Journal of The Chemical Society

DETROIT PUBLIC LIBRARY
NOV 29 1961
TECHNOLOGY DEPARTMENT

October 1961

XUM

PUBLICATION COMMITTEE

Chairman

D. H. Hey, D.Sc., F.R.I.C., F.R.S.

G. O. Aspinall, D.Sc., F.R.S.E., F.R.I.C.
Wilson Baker, M.A., D.Sc., F.R.S.
J. W. Barrett, Ph.D., A.R.C.S., F.R.I.C.
R. P. Bell, M.A., F.R.S.
E. Boyland, D.Sc., Ph.D.
D. M. Brown, Ph.D.
G. M. Burnett, Ph.D., D.Sc.
I. G. M. Campbell, B.Sc., Ph.D.
N. Campbell, D.Sc., Ph.D.
N. B. Chapman, M.A., Ph.D., F.R.I.C.
J. Chatt, M.A., Sc.D., F.R.I.C., F.R.S.
D. D. Eley, Sc.D., Ph.D.
D. H. Everett, M.B.E., M.A., D. Phil.
R. H. Hall, Ph.D., A.R.C.S., F.R.I.C.
T. G. Halsall, Ph.D., M.A., A.R.I.C.
D. J. G. Ives, D.Sc., A.R.C.S., F.R.I.C.
A. W. Johnson, Sc.D., Ph.D., A.R.C.S.
C. Kemball, M.A., Ph.D., F.R.I.C.
J. A. Kitchener, D.Sc., Ph.D.
G. Kohnstam, Ph.D.
H. C. Longuet-Higgins, M.A., D.Phil., F.R.S
B. Lythgoe, M.A., Ph.D., F.R.I.C., F.R.S.
H. T. Openshaw, M.A., D.Phil.
R. A. Raphael, D.Sc., A.R.C.S., F.R.I.C.
P. L. Robinson, D.Sc., F.R.I.C.
K. Schofield, Ph.D., D.Sc., F.R.I.C.
A. G. Sharpe, M.A., Ph.D., F.R.I.C.
J. C. Speakman, M.Sc., Ph.D., D.Sc.
K. W. Sykes, M.A., D.Phil.
Sir Alexander Todd, M.A., D.Sc., F.R.S.
B. C. L. Weedon, D.Sc., A.R.C.S., F.R.I.C.
D. H. Whiffen, M.A., D.Phil.
M. C. Whiting, M.A., Ph.D., A.R.C.S.
G. Wilkinson, Ph.D., A.R.C.S.

Editor

R. S. Cahn, M.A., D.Phil.Nat., F.R.I.C.

Deputy Editor

L. C. Cross, Ph.D., A.R.C.S., F.R.I.C.

Assistant Editors

A. D. Mitchell, D.Sc., F.R.I.C. I. J. Cantlon, Ph.D.

Subscription rate to non-Fellows £20 0s. 0d. (including Proceedings) per annum post free.

XUM

XUM

XUM

CONTENTS

General, physical, and inorganic

NO.		PAGE
841	Complexes of transition metals with a tetra-tertiary arsine By G. A. BARCLAY and A. K. BARNARD	4269
860	Thermodynamics of ion association. Part VIII. Some transition-metal malonates By V. S. K. NAIR and G. H. NANCOLLAS	4367
862	The crystal and molecular structure of 3-methylbenzothiazoline-2-thione By P. J. WHEATLEY	4379
867	Mesityl and phenyl derivatives of lead By F. GLOCKLING, K. HOOTON, and D. KINGSTON	4405
873	Tritertiary arsine complexes of nickel, palladium, and platinum By G. A. BARCLAY, R. S. NYHOLM, and R. V. PARISH	4433
874	High-temperature studies of the system calcium oxide–phosphorus pentoxide By J. H. WELCH and W. GUTT	4442
875	Deformation frequencies of OH groups in nitrosylruthenium complexes By D. SCARGILL	4444
877	Metal–metal interactions in square-planar complexes By J. R. MILLER	4452
878	Thermodynamics of ion association. Part IX. Some transition-metal succinates By A. MCAULEY and G. H. NANCOLLAS	4458
883	Effect of pressure on the transport of non-electrolytes through ion-selective membranes By J. W. JARVIS and F. L. TYE	4483
899	The structure of complex molybdenum(III) thiocyanates By J. LEWIS, R. S. NYHOLM, and P. W. SMITH	4590
906	Spectrophotometric and thermodynamic properties of some copper and iron complexes By B. R. JAMES, M. PARRIS, and R. J. P. WILLIAMS.	4630
907	The mechanism and steric course of octahedral aquation. Part IV. The aquation of *cis*- and *trans*-dichloro- and *cis*- and *trans*-chlorohydroxo-bis(ethylenediamine)-cobalt(III) salts By M. E. BALDWIN, S. C. CHAN, and M. L. TOBE	4637

NOTES

917	The first acid dissociation constant of hydrogen sulphide at high pressures By A. J. ELLIS and D. W. ANDERSON	4678
918	Interaction of trialkyl phosphates with silicon chlorides By M. J. FRAZER, W. GERRARD, and A. P. SINGH	4680
923	The preparation of silver fluoroborate and silver hexafluorophosphate By D. R. RUSSELL and D. W. A. SHARP	4689

Physical organic

842	The electron-spin resonance spectra and odd-electron distribution of a number of polycyclic semiquinones and their derivatives By R. W. BRANDON and E. A. C. LUCKEN	4273
843	The reactions of hydroxyl radicals with hydrocarbons in aqueous solution By T. BÉRCES and A. F. TROTMAN-DICKENSON	4281
844	Competitive oxidations. Part III. Oxidations at low temperatures induced by light By W. E. FALCONER, J. H. KNOX, and A. F. TROTMAN-DICKENSON	4285

XUM

NO. PAGE

845 The acid and alkaline hydrolysis of some substituted phenyl α-D-glucosides
By A. N. HALL, SHEILA HOLLINGSHEAD, and H. N. RYDON 4290

852 The existence of the P^1P^1-diethyl pyrophosphate ion
By DAVID SAMUEL and B. SILVER 4321

854 Heterocyclic derivatives of guanidine. Part III. Stoicheiometry and kinetics of the condensation of ethyl cyanoacetate with guanidino-2*H*-pyrroles
By J. E. BANFIELD 4332

855 Concomitant first- and second-order nucleophilic substitution
By P. CASAPIERI and E. R. SWART 4342

859 The hydrolysis of acetic anhydride. Part VII. Catalysis by pyridine and methylpyridines in acetate buffers
By A. R. BUTLER and V. GOLD 4362

863 The structure of isoclovene: *X*-ray analysis of the hydrochloride and hydrobromide
By J. S. CLUNIE and J. MONTEATH ROBERTSON 4382

865 Solvation of ions. Part III. The S_N2 reactivity of some Group VI anions, pyridine, and alkyl halides in dipolar aprotic solvents
By A. J. PARKER 4398

866 The reaction of methylene with buta-1,3-diene
By BARBARA GRZYBOWSKA, J. H. KNOX, and A. F. TROTMAN-DICKENSON . . 4402

876 Molecular polarisability: the conformations of biacetyl, benzil, and furil as solutes in benzene or carbon tetrachloride
By (MISS) P. H. CURETON, (MRS.) C. G. LE FÈVRE, and R. J. W. LE FÈVRE . 4447

891 Electric dipole moments of substituted pyridines, pyridine 1-oxides, and nitrobenzenes
By A. N. SHARPE and S. WALKER 4522

905 The concerted action of fluoride and silver ions on diethyl ethylphosphonothiolate in aqueous solution
By B. SAVILLE 4624

910 The catalytic action of anionic catalysts. Part I. The interaction of butyllithium with 1,1,-diphenylethylene
By ALWYN G. EVANS and DAVID B. GEORGE 4653

Organic

846 The reaction of ethyl 2-oxocyclopentanecarboxylate with arylamines. Part I. The preparation of 2,3-dihydro-α-quinindones (2,3,4,5-tetrahydro-4-oxo-1*H*-cyclopenta[*c*]quinolines)
By R. J. BROWN, F. W. S. CARVER, and B. L. HOLLINGSWORTH. 4295

847 The polymerization of epoxides. Part III. The polymerization of propylene oxide by sodium alkoxides
By GEOFFREY GEE, W. C. E. HIGGINSON, K. J. TAYLOR, and M. W. TRENHOLME . 4298

848 The interaction of decalin and isobutyryl chloride–aluminium chloride
By M. S. AHMAD and G. BADDELEY 4303

849 The interaction of decalin, propionyl chloride, and aluminium chloride
By G. BADDELEY and B. G. HEATON 4306

850 The structure of bassic acid
By T. J. KING and J. P. YARDLEY 4308

851 Polynitronaphthalenes. Part III. A quantitative study of the further nitration of the ten dinitronaphthalenes
By E. R. WARD and C. D. JOHNSON 4314

853 The rôle of peroxides in the autoxidation of elaidic acid and oleic esters
By GEORGE KING 4324

856 Organophosphorus compounds. Part III. Reactions of the alkali derivatives of dialkyl phosphites
By ZVI PELCHOWICZ, SARAH BRUKSON, and ERNST D. BERGMANN 4348

857 A synthesis of 1-ethyl-1,2,3,5-tetrahydro-10-methyl-7,8-methylenedioxy-5-oxobenzo[*f*]pyrrocoline, a degradation product of lycorine
By SHUZO TAKAGI and SHOJIRO UYEO 4350

XUM

NO.		PAGE
858	An examination of the rutaceae of Hong Kong. Part VIII. The synthesis of the alkaloid, graveoline By H. R. Arthur and (Miss) Lucy Y. S. Loh	4360
861	Amino-acids of the cyclohexane series. Part I By L. Munday	4372
864	Organic peroxides. Part X. The autoxidation of ethyl chaulmoograte: the course and stereochemistry of homolytic autoxidation By Alwyn G. Davies and J. E. Packer	4390
868	Syntheses of long-chain acids. Part II. A synthesis of linoleic acid By D. E. Ames and P. J. Islip	4409
869	Pteridine studies. Part XIV. Methylation of 2-amino-4-hydroxypteridine and related compounds By D. J. Brown and N. W. Jacobsen	4413
870	Maytenone. Part I. Isolation and structural studies By A. W. Johnson, T. J. King, and R. J. Martin	4420
871	The synthesis of 8-isopropylpodocarpane-6,7-diol (6-hydroxytotarol) and of 7,8-dimethoxypodocarpane By N. F. Elmore and T. J. King	4425
872	The synthesis of podocarpane-6,7-diol, a degradation product of maytenone By J. A. Hill, A. W. Johnson, and T. J. King	4430
879	β-Glucopyranosides of hydroxymethyl- and hydroxyethyl-ferrocene By A. N. de Belder, E. J. Bourne, and J. B. Pridham	4464
880	The synthesis of 8-substituted purines By F. Bergmann and M. Tamari	4468
881	Reactions of ketones with oxidising agents. Part I. Catalysis of the ketone–lead tetra-acetate reaction with boron trifluoride By H. B. Henbest, D. N. Jones, and G. P. Slater	4472
882	Aspects of stereochemistry. Part XVIII. Synthesis of the 10-methyldecalin-2,9-diols By H. B. Henbest and J. McEntee	4478
884	Radiation chemistry of organic halogen compounds. Part I. The action of γ-radiation on chlorinated ethylenes By W. Miller, (the late) W. H. Stafford, W. H. Taylor, D. Leaver, and A. H. McQuillan	4485
885	Pyrone series. Part IV. 5-Aryloxy-2-pyrones. The corresponding 2-thiopyrones, pyridones, 1-hydroxy- and 1-amino-2-pyridones, and related 4,5,6-triphenyl-2-pyrones By Ibrahim El-Sayed El-Kholy, Fathi Kamel Rafla, and Gabra Soliman	4490
886	Photodimers of alkylbenzoquinones By R. C. Cookson, D. A. Cox, and J. Hudec	4499
887	Lignans. Part I. Acylation in polyphosphoric acid as a route to intermediates By D. C. Ayres and R. C. Denney	4506
888	The action of sulphur monochloride on aromatic hydrocarbons By Z. S. Ariyan and L. A. Wiles	4510
889	The action of aluminium chloride on some *o*-alkylbenzenesulphonic acids and *o*-alkyldiphenyl sulphones By G. Holt and B. Pagdin	4514
890	Cyanohydrins of ethyl γγγ-trifluoroacetoacetate and 5,5,5-trifluoro-4-oxopentanoic acid By J. Burdon, T. J. Smith, and J. C. Tatlow	4519
892	Compounds related to the steroid hormones. Part III.[1] Phenolic ethers from the dienone–phenol rearrangement of $\Delta^{1,4}$-3-oxo-steroids By J. Elks, J. F. Oughton, and L. Stephenson	4531
893	Compounds related to the steroid hormones. Part IV. Dienone–phenol rearrangement of steroid $\Delta^{1,4}$-3,11-diketones By (Miss) E. J. Bailey, J. Elks, J. F. Oughton, and L. Stephenson	4535

XUM

NO.		PAGE
894	Compounds related to the steroid hormones. Part V. The partial synthesis of 21-acetoxy-17-hydroxy-16β-methyl-5α-pregn-9-ene-3,20-dione By J. Attenburrow, J. E. Connett, W. Graham, J. F. Oughton, A. C. Ritchie, and P. A. Wilkinson	4547
895	Compounds related to the steroid hormones. Part VI. The synthesis of the 9α-fluoro-16β-methyl derivatives of hydrocortisone and prednisolone By T. R. Carrington, S. Eardley, J. Elks, G. F. H. Green, G. I. Gregory, A. G. Long, and J. C. P. Sly	4560
896	Compounds related to the steroid hormones. Part VII. Preparation of $\Delta^{9(11)}$-steroids from 11β-trifluoroacetates By J. Elks and G. H. Phillipps	4573
897	The mechanism of hydramine fission By A. Chatterjee, S. K. Srimany, and (Miss) B. Chaudhury	4576
898	The chemistry of fungi. Part XXXIX. The structure of monascin By B. C. Fielding, J. S. E. Holker, D. F. Jones, A. D. G. Powell, K. W. Richmond, Alexander Robertson, and W. B. Whalley	4579
900	Ferrocene derivatives. Part VIII. Tetrahydropyridoferrocenes By J. M. Osgerby and P. L. Pauson	4600
901	Ferrocene derivatives. Part IX. Some disubstituted derivatives By J. M. Osgerby and P. L. Pauson	4604
902	Ferrocene derivatives. Part X. Their preparation from fulvenes By G. R. Knox and P. L. Pauson	4610
903	Ferrocene derivatives. Part XI. Azoferrocenes By G. R. Knox and P. L. Pauson	4615
904	Some substituted cyclopentadienyl derivatives of nickel, cobalt, iron, molybdenum, and titanium By G. R. Knox, J. D. Munro, P. L. Pauson, G. H. Smith, and W. E. Watts	4619
908	*Solanum* alkaloids. Part XV. The constituents of some *Solanum* species and a reassessment of solasodamine and solauricine By Lindsay H. Briggs, R. C. Cambie, and J. L. Hoare	4645
909	Ionophoresis of carbohydrates. Part VII. 2,5-Di-*O*-methyl-L-rhamnose: its ionophoresis and conversion into 6-deoxy-2,5-di-*O*-methyl-L-altrose By A. B. Foster, J. Lehmann, and M. Stacey	4649
911	The synthesis of 3-alkyl-1-arylsulphonyl-hydantoins and -2-thiohydantoins By G. Holan and E. Samuel	4660
912	Polymerisation of flavans. Part V. The stereochemistry of 2,3-*trans*-flavan-3,4-diols By M. M. Bokadia, B. R. Brown, P. L. Kolker, C. W. Love, J. Newbould, G. A. Somerfield, and P. M. Wood	4663
	NOTES	
913	Organic fluorine compounds. Part XXVI. Synthesis of α-fluoro-β-alanine By Ernst D. Bergmann and Sasson Cohen	4669
914	Heterocyclic derivatives of guanidine. Part IV By J. E. Banfield	4672
915	The characterisation of amines by use of (−)-di-*O*-*p*-toluoyltartaric acid By D. A. A. Kidd	4675
916	Steroids of unnatural configuration. Part VI. Oxidation and reduction of epilumisterol By G. D. Meakins and M. W. Pemberton	4676
919	Hydroxyanthracene series. Part IV. Synthesis of some anthraquinone derivatives By N. H. Shah and Suresh Sethna	4682
920	Constituents of *Eugenia maire* A. Cunn. Part II. Identification of mairin and constituents of the leaves By Lindsay H. Briggs and R. C. Cambie	4684

NO. PAGE

921 The direct amination of mesitylene by hydrazoic acid in concentrated sulphuric acid
By G. M. Hoop and J. M. Tedder 4685

922 Some compounds derived from *o*-2-carboxyethylbenzoic acid
By E. D. Andrews and W. E. Harvey 4687

924 The reaction between furfuryl alcohol and 2,4-dinitrophenylhydrazine in methanolic hydrochloric acid
By K. G. Lewis 4690

925 The synthesis of 4,5,7-trimethoxy-2-propylanthraquinone
By A. J. Birch and C. J. Moye 4691

926 The synthesis of (±)-*S*-3-methylbut-2-enylhomocysteine
By A. J. Birch and M. Slaytor 4692

INDEX OF AUTHORS' NAMES

Ahmad, M. S., and Baddeley, G., 4303
Ames, D. E., and Islip, P. J., 4409
Anderson, D. W. See Ellis, A. J., 4678
Andrews, E. D., and Harvey, W. E., 4687
Ariyan, Z. S., and Wiles, L. A., 4510
Arthur, H. R., and Loh, L. Y. S., 4360
Attenburrow, J., Connett, J. E., Graham, W., Oughton, J. F., Ritchie, A. C., and Wilkinson, P. A., 4547
Ayres, D. C., and Denney, R. C., 4506
Baddeley, G., and Heaton, B. G., 4306
Baddeley, G. See also Ahmad, M. S., 4303
Bailey, E. J., Elks, J., Oughton, J. F., and Stephenson, L., 4535
Baldwin, M. E., Chan, S. C., and Tobe, M. L., 4637
Banfield, J. E., 4332, 4672
Barclay, G. A., and Barnard, A. K., 4269
Barclay, G. A., Nyholm, R. S., and Parish, R. V., 4433
Barnard, A. K. See Barclay, G. A., 4269
de Belder, A. N., Bourne, E. J., and Pridham, J. B., 4464
Bérces, T., and Trotman-Dickenson, A. F., 4281
Bergmann, E. D., and Cohen, S., 4669
Bergmann, E. D. See also Pelchowicz, Z., 4348
Bergmann, F., and Tamari, M., 4468
Birch, A. J., and Moye, C. J., 4691
Birch, A. J., and Slaytor, M., 4692
Bokadia, M. M., Brown, B. R., Kolker, P. L., Love, C. W., Newbould, J., Somerfield, G. A., and Wood, P. M., 4663
Bourne, E. J. See de Belder, A. N., 4464
Brandon, R. W., and Lucken, E. A. C., 4273
Briggs, L. H., and Cambie, R. C., 4684
Briggs, L. H., Cambie, R. C., and Hoare, J. L., 4645
Brown, B. R. See Bokadia, M. M., 4663
Brown, D. J., and Jacobsen, N. W., 4413.
Brown, R. J., Carver, F. W. S., and Hollingsworth, B. L., 4295
Brukson, S. See Pelchowicz, Z., 4348
Burdon, J., Smith, T. J., and Tatlow, J. C., 4519
Butler, A. R., and Gold, V., 4362
Cambie, R. C. See Briggs, L. H., 4645, 4684
Carrington, T. R., Eardley, S., Elks, J., Green, G. F. H., Gregory, G. I., Long, A. G., and Sly, J. C. P., 4560
Carver, F. W. S. See Brown, R. J., 4295
Casapieri, P., and Swart, E. R., 4342
Chan, S. C. See Baldwin, M. E., 4637
Chatterjee, A., Srimany, S. K., and Chaudhury, B., 4576
Chaudhury, B. See Chatterjee, A., 4576
Clunie, J. S., and Robertson, J. M., 4382
Cohen, S. See Bergmann, E. D., 4669
Cookson, R. C., Cox, D. A., and Hudec, J., 4499
Connett, J. E. See Attenburrow, J., 4547
Cox, D. A. See Cookson, R. C., 4499
Cureton, P. H., Le Fèvre, C. G., and Le Fèvre, R. J. W., 4447
Davies, A. G., and Packer, J. E., 4390
Denney, R. C. See Ayres, D. C., 4506
Eardley, S. See Carrington, T. R., 4560
El-Kholy, I. El-S., Rafla, F. K., and Soliman, G., 4490
Elks, J., Oughton, J. F., and Stephenson, L., 4531
Elks, J., and Phillipps, G. H., 4573
Elks, J. See also Bailey, E. J., 4535, and Carrington, T. R., 4560
Ellis, A. J., and Anderson, D. W., 4678
Elmore, N. F., and King, T. J., 4425
Evans, A. G., and George, D. B., 4653
Falconer, W. E., Knox, J. H., and Trotman-Dickenson, A. F., 4285
Fielding, B. C., Holker, J. S. E., Jones, D. F., Powell, A. D. G., Richmond, K. W., Robertson, A., and Whalley, W. B., 4579
Foster, A. B., Lehmann, J., and Stacey, M., 4649
Frazer, M. J., Gerrard, W., and Singh, A. P., 4680
Gee, G., Higginson, W. C. E., Taylor, K. J., and Trenholme, M. W., 4298
George, D. B. See Evans, A. G., 4653
Gerrard, W. See Frazer, M. J., 4680
Glockling, F., Hooton, K., and Kingston, D., 4405
Gold, V. See Butler, A. R., 4362
Graham, W. See Attenburrow, J., 4547
Green, G. F. H. See Carrington, T. R., 4560
Gregory, G. I. See Carrington, T. R., 4560
Grzybowska, B., Knox, J. H., and Trotman-Dickenson, A. F., 4402
Gutt, W. See Welch, J. H., 4442
Hall, A. N., Hollingshead, S., and Rydon, H. N., 4290
Harvey, W. E. See Andrews, E. D., 4687
Heaton, B. G. See Baddeley, G., 4303
Henbest, H. B., Jones, D. N., and Slater, G. P., 4472

XUM

Henbest, H. B., and McEntee, J., 4478
Higginson, W. C. E. See Gee, G., 4298
Hill, J. A., Johnson, A. W., and King, T. J., 4430
Hoare, J. L. See Briggs, L. H., 4645
Holan, G., and Samuel, E., 4660
Holker, J. S. E. See Fielding, B. C., 4579
Hollingshead, S. See Hall, A. N., 4290
Hollingsworth, B. L. See Brown, R. J., 4295
Holt, G., and Pagdin, B., 4514
Hoop, G. M., and Tedder, J. M., 4685
Hooton, K. See Glockling, F., 4405
Hudec, J. See Cookson, R. C., 4499
Islip, P. J. See Ames, D. E., 4409
Jacobsen, N. W. See Brown, D. J., 4413
James, B. R., Parris, M., and Williams, R. J. P., 4630
Jarvis, J. W., and Tye, F. L., 4483
Johnson, A. W., King, T. J., and Martin, R. J., 4420
Johnson, A. W. See also Hill, J. A., 4430
Johnson, C. D. See Ward, E. R., 4314
Jones, D. F. See Fielding, B. C., 4579
Jones, D. N. See Henbest, H. B., 4472
Kidd, D. A. A., 4675
King, G., 4324
King, T. J., and Yardley, J. P., 4308
King, T. J. See also Elmore, N. F., 4425, Hill, J. A., 4430, and Johnson, A. W., 4420
Kingston, D. See Glockling, F., 4405
Knox, G. R., Munro, J. D., Pauson, P. L., Smith, G. H., and Watts, W. E., 4619
Knox, G. R., and Pauson, P. L., 4610, 4615
Knox, J. H. See Falconer, W. E., 4285, and Grzybowska, B., 4402
Kolker, P. L. See Bokadia, M. M., 4663
Leaver, D. See Miller, W., 4485
Le Fèvre, C. G. See Cureton, P. H., 4447
Le Fèvre, R. J. W. See Cureton, P. H., 4447
Lehmann, J. See Foster, A. B., 4649
Lewis, J., Nyholm, R. S., and Smith, P. W., 4590
Lewis, K. G., 4690
Loh, L. Y. S. See Arthur, H. R., 4360
Long, A. G. See Carrington, T. R., 4560
Love, C. W. See Bokadia, M. M., 4663
Lucken, E. A. C. See Brandon, R. W., 4273
McAuley, A., and Nancollas, G. H., 4458
McEntee, J. See Henbest, H. B., 4478
McQuillan, A. H., 4485
Martin, R. J. See Johnson, A. W., 4420
Meakins, G. D., and Pemberton, M. W., 4676
Miller, J. R., 4452
Miller, W., Stafford, W. H., Taylor, W. H., Leaver, D., and McQuillan, A. H., 4485
Moye, C. J. See Birch, A. J., 4691
Munday, L., 4372
Munro, J. D. See Knox, G. R., 4619
Nair, V. S. K., and Nancollas, G. H., 4367
Nancollas, G. H. See McAuley, A., 4458, and Nair, V. S. K., 4367
Newbould, J. See Bokadia, M. M., 4663
Nyholm, R. S. See Barclay, G. A., 4433, and Lewis, J., 4590
Osgerby, J. M., and Pauson, P. L., 4600, 4604
Oughton, J. F. See Attenburrow, J., 4547, Bailey, E. J., 4535, and Elks, J., 4531
Packer, J. E. See Davies, A. G., 4390
Pagdin, B. See Holt, G., 4514
Parish, R. V. See Barclay, G. A., 4433
Parker, A. J., 4398
Parris, M. See James, B. R., 4630
Pauson, P. L. See Knox, G. R., 4610, 4615, 4619, and Osgerby, J. M., 4600, 4604
Pelchowicz, Z., Brukson, S., and Bergmann, E. D., 4348
Pemberton, M. W. See Meakins, G. D., 4676
Phillipps, G. H. See Elks, J., 4573
Powell, A. D. G. See Fielding, B. C., 4579
Pridham, J. B. See de Belder, A. N., 4464
Rafla, F. K. See El-Kholy, I. El-S., 4490
Richmond, K. W. See Fielding, B. C., 4579
Ritchie, A. C. See Attenburrow, J., 4547
Robertson, A. See Fielding, B. C., 4579
Robertson, J. M. See Clunie, J. S., 4382
Russell, D. R., and Sharp, D. W. A., 4689
Rydon, H. N. See Hall, A. N., 4290
Samuel, D., and Silver, B., 4321
Samuel, E. See Holan, G., 4660
Saville, B., 4624
Scargill, D., 4444
Sethna, S. See Shah, N. H., 4682
Shah, N. H., and Sethna, S., 4682
Sharp, D. W. A. See Russell, D. R., 4689
Sharpe, A. N., and Walker, S., 4522
Silver, B. See Samuel, D., 4321
Singh, A. P. See Frazer, M. J., 4680
Slater, G. P. See Henbest, H. B., 4472
Slaytor, M. See Birch, A. J., 4692
Sly, J. C. P. See Carrington, T. R., 4560
Smith, G. H. See Knox, G. R., 4619
Smith, P. W. See Lewis, J., 4590
Smith, T. J. See Burdon, J., 4519
Soliman, G. See El-Kholy, I. El-S., 4490
Somerfield, G. A. See Bokadia, M. M., 4663
Srimany, S. K. See Chatterjee, A., 4576
Stacey, M. See Foster, A. B., 4649
Stafford, W. H. See Miller, W., 4485
Stephenson, L. See Bailey, E. J., 4535, and Elks, J., 4531
Swart, E. R. See Casapieri, P., 4342
Takagi, S., and Uyeo, S., 4350
Tamari, M. See Bergmann, F., 4468
Tatlow, J. C. See Burdon, J., 4519
Taylor, K. J. See Gee, G., 4298
Taylor, W. H. See Miller, W., 4485
Tedder, J. M. See Hoop, G. M., 4685
Tobe, M. L. See Baldwin, M. E., 4637
Trenholme, M. W. See Gee, G., 4298
Trotman-Dickenson, A. F. See Bérces, T., 4281, Falconer, W. E., 4285, and Grzybowska, B., 4402
Tye, F. L. See Jarvis, J. W., 4483
Uyeo, S. See Takagi, S., 4350
Walker, S. See Sharpe, A. N., 4522
Ward, E. R., and Johnson, C. D., 4314
Watts, W. E. See Knox, G. R., 4619
Welch, J. H., and Gutt, W., 4442
Whalley, W. B. See Fielding, B. C., 4579
Wheatley, P. J., 4379
Wiles, L. A. See Ariyan, Z. S., 4510
Wilkinson, P. A. See Attenburrow, J., 4547
Williams, R. J. P. See James, B. R., 4630
Wood, P. M. See Bokadia, M. M., 4663
Yardley, J. P. See King, T. J., 4308

XUM

PAPERS ACCEPTED

Substituted benzidines and related compounds as reagents in analytical chemistry. Part XVII. The *NNN'N'*-tetracarboxymethyl derivatives of some 3,3'-disubstituted benzidines. By D. I. Rees and W. I. Stephen

Controlled potential electrolysis. Part VII. Polarographic behaviours and controlled potential electrolysis of 1,1-dinitroethane and dinitromethane. By Masaichiro Masui and Hiroteru Sayo

A comparison of the nucleophilic reactivity of ethoxide, methoxide, and hydroxide ions in dioxan. By (Miss) I. R. Alet and B. D. England

Iodomercurate complexes with Group V quaternary iodides. Part II. Reactions with triphenylphosphine. By G. B. Deacon and B. O. West

Isomer ratios for the mononitration of *p*-terphenyl in acetic acid and acetic anhydride. By C. W. Gray and D. Lewis

Constituents of the higher fungi. Part I. Hispidin, a new 4-hydroxy-6-styrylpyrone from *Polyporus hispidus* (Bull.) Fr. By R. L. Edwards, D. C. Lewis, and D. V. Wilson

Electron-spin resonance investigations of the negative ions of four organosilicon compounds. By M. G. Townsend

The reaction of nicotinic acid *N*-oxide and 3-picoline *N*-oxide with acetic anhydride. By B. M. Bain and J. E. Saxton

The stability of dicalcium phosphate precipitated from solutions of calcium nitrate and phosphoric acid. By D. H. Booth and R. V. Coates

Polysaccharides of the characeae. Part IV. A non-esterified pectic acid from *Nitella translucens*. By D. M. W. Anderson and N. J. King

Studies on uronic acid materials. Part IV. Aqueous decarboxylation of uronic acids, and the decarboxylation of pectic materials during extraction. By D. M. W. Anderson, A. M. Bews, S. Garbutt, and N. J. King

Dipole moments, and absorption spectra of 4-arylazo-1-naphthylamines. By D. A. Ibbitson, P. C. James, and R. A. Knaust

The composition of *Afraegle paniculata* mucilage. By F. G. Torto

The oxidation of organic sulphides. Part X. The co-oxidation of sulphides and olefins. By D. Barnard, L. Bateman, M. E. Cain, T. Colclough, and J. I. Cunneen

Glow-discharge electrolysis. Part IV. The formation of hydrazine in liquid ammonia. By A. Hickling and C. R. Newns

Glow-discharge electrolysis. Part V. The contact glow-discharge electrolysis of liquid ammonia. By A. Hickling and G. R. Newns

Reactions of some substituted benzo-1,2,3-triazines. By E. W. Parnell

The preparation and properties of disilyl cyanamide. By E. A. V. Ebsworth and M. J. Mays

The dielectric polarization of some imperfect polar gases. By A. D. Buckingham and R. E. Raab

The mechanism of solvolysis of γ-phenyltetronic acid enol esters. Part I. A conductometric study of the methanolysis of γ-phenyltetronic acid enol benzoate. By Alicja Kirkien-Konasiewicz and Allan Maccoll

Chemistry of some derivatives of *S*-(2-hydroxyethyl) thioureas. By L. A. Cort

The spectra of inorganic complexes in non-aqueous solvents. Part I. Chlorocobaltate ion and cobalt chloride. By S. Buffagni and T. M. Dunn

The crystal and molecular structure of biphenylene. By T. C. W. Mak and J. Trotter

The reactivity of organophosphorus compounds. Part VIII. The reactions of chloramine-T with triethyl phosphorothiolate and related compounds. By J. I. C. Cadogan and H. N. Moulden

The reactivity of organophosphorus compounds. Part IX. The reaction of thionates with alkyl iodides. By A. J. Burn and J. I. C. Cadogan

The preparation of ammonium alkyl hydrogen phosphites. By T. D. Smith

The initiation step in the polymerization of n-carboxy-α-amino-acid anhydrides. Part I. Catalysis by tertiary base. By C. H. Bamford and H. Block

The initiation step in the polymerization of *N*-carboxy-α-amino-acid anhydrides. Part II. Effects related to the structure of amine initiators. By C. H. Bamford and H. Block

Characterisation of sugars as *p*-*p'*-nitrophenylazobenzoyl derivatives. By El S. Amin

Condensation of ethyl pyridyl-2- and -4-acetates with aromatic carbonyl compounds. By D. R. Bragg and D. G. Wibberley

XUM

Initial thermoelectric power measurements on thermocells with iodine–iodide electrodes at a mean temperature of 30° C. By H. J. V. TYRELL and P. J. WILSON

Friedel–Crafts acylation, with stannic chloride as catalyst, in solvents of low dielectric constant. By D. P. N. SATCHELL

Organic peroxides. Part VI. The decomposition of *p*-nitrophenyldiphenylmethyl peroxides. By J. I. G. CADOGAN, D. H. HEY, and W. A. SANDERSON

Bisquaternary salts related to quinapyramine (antrycide). Replacement of the quinoline nucleus by other heterocycles. By S. S. BERG and E. W. PARNELL

Pteridine studies. Part XV. The reduction of 2-hydroxypteridine. By A. ALBERT and S. MATSUURA

The disproportionation of carbodi-imides. By I. G. HINTON and R. F. WEBB

Synthetic and stereochemical studies in the perhydrobenzocyclohepten-1-one system. By DVORA KIMCHI and SHLOMO BIEN

Activity coefficients of non-electrolytes in aqueous solutions of sugars. By A. GRAHAM FOSTER and I. E. SIDDIQI

The oxidation of ethers and related compounds. Part I. The thermal and photochemical decomposition of t-butyl peroxide in anisole. By H. B. HENBEST, J. A. W. REID, and C. J. M. STIRLING

Aromatic reactivity. Part XX. Diphenyl ether, diphenyl sulphide, dibenzofuran, and dibenzothiophen in detritiation. By R. BAKER and C. EABORN

The kinetics and mechanisms of aromatic halogen substitution. Part XI. Chlorination of phenanthrene in acetic acid. By P. B. D. DE LA MARE, N. V. KLASSEN, and (in part) R. KOENIGSBERGER

Thiosuccinimides. By R. J. W. CREMLYN

The reactions of hexamethyldisilthiane and ethylthiotrimethylsilane with alcohols, thiols, acids, and amines. By E. W. ABEL

An *X*-ray determination of the crystal and molecular structure of perchlorofulvalene. By P. J. WHEATLEY

The rôle of supports in catalytic hydrogenation. Part II. Further effects of various oxide supports on the activity of platinum. By E. B. MAXTED and J. S. ELKINS

Thermochemical studies. Part VI. Heats and entropies of reaction of transition-metal ions with triethylenetetramine. By L. SACCONI, P. PAOLETTI, and M. CIAMPOLINI

Phosphino-arylboranes. By G. E. COATES and J. G. LIVINGSTONE

Aminoditolylborane and the preparation of diarylborinic acids. By G. E. COATES and J. G. LIVINGSTONE

Estimation of the relative amounts of isomeric sulphate esters in some sulphated polysaccharides. By D. A. REES

Heterocyclic compounds from urea derivatives. Part II. Synthesis and cyclisation of 4-substituted 1-amidino-semicarbazides and -thiosemicarbazides. By LEONARD E. A. GODFRY and FREDERICK KURZER

Polycyclic cinnoline derivatives. Part IX. The bromination of benzo[*c*]cinnoline and the preparation and ultraviolet absorption spectra of reference compounds. By J. F. CORBETT and P. F. HOLT

Reactions at position 1 of carbohydrates. Part II. The variation of optical rotation of some aryl glucosides with temperature. By B. CAPON, W. G. OVEREND, and M. SOBELL

Evidence for a single-stage two-electron exchange in the thallous–thallic reaction. By A. G. SYKES

The thermal isomerization of spiro-pentane. By H. M. FREY

Aucubin. By A. J. BIRCH, J. GRIMSHAW, and H. R. JUNEJA

Thiophthalimides. By R. J. W. CREMLYN

Some unusual reactions of toluene-*p*-sulphonhydrazide.. By A. DEAVIN and C. W. REES

" Barnes's tetrahydroindenoindene " derivatives: two spiroindanes. By R. F. CURTIS and K. O. LEWIS

Manganese(II) chloride complexes. Part I. Stability constants. By D. F. C. MORRIS and E. L. SHORT

The chemistry of triterpenes and related compounds. Part XLI. The bromination of lupeol and its esters. By S. R. GUPTA, T. G. HALSALL, and E. R. H. JONES

Carbonic esters of sucrose. Part I. The preparation of *O*-alkyloxycarbonylsucroses. By R. S. THEOBALD

Carbonic esters of sucrose. Part II. The polymerisation of *O*-alkyloxycarbonylsucroses. By R. S. THEOBALD

Carbonic esters of sucrose. Part III. The direct preparation of poly(sucrose carbonates) from sucrose. By R. S. THEOBALD

XUM

Purines, pyrimidines, and imadazoles. Part XVI. Some 1-aminoimidazoles and derived 9-aminopurines. By R. N. Naylor, G. Shaw, D. V. Wilson, and (in part) D. N. Butler
New syntheses of trisulphides. By B. Milligan, B. Saville, and J. M. Swan
The structure and stereochemistry of sumatrol and malaccol. By L. Crombie and R. Peace
Dehydrogenation with mercuric acetate in the lupane series. Part II. Lupeol and derivatives. By J. M. Allison, W. Lawrie, J. McLean, and (in part) J. M. Beaton
Counter-ion fixation in alginates. By A. Katchalsky, R. E. Cooper, J. Upadhyay, and A. Wassermann
The polarographic reduction of some heterocyclic molecules. Part III. Quinoline ethiodide. By D. J. Casimir, A. J. Harle, and L. E. Lyons
12-Benzyl- and 12-alkyl-6-aminochrysenes. By P. Mabille and N. P. Buu-Hoï
The hemicelluloses of roselle fibre (*Hibiscus sabdariffa*). By P. C. Das Gupta
Action of thionyl chloride upon alcohols derived from alpha- and beta-prodine. By A. F. Casy
Tanshinones. Part I. The synthesis of an isomer of tanshinone-I. By T. J. King and G. Read
The crystal structure of monopyridinecopper(II) acetate. By G. A. Barclay and C. H. L. Kennard
N-Alkylated 5-fluorotryptamines. By Z. Pelchowicz, A. Kaluszyner, and M. Bentov
The base-catalysed isomerisation of some 3-alkyldihydroanisoles. By A. J. Birch, (Mrs.) E. M. A. Shoukry, and F. Stansfield
The reactivity of organophosphorus compounds. Part X. The reaction of phosphorothiolates with alkyl iodides. By A. J. Burn, J. I. G. Cadogan, and H. N. Moulden
Synthesis of 3-*O*-*p*-coumaroylquinic acid. By E. Haslam, R. D. Haworth, and G. K. Makinson
Molecular polarisability. Phenylpolyenals and diphenylpolyene ketones. By R. Bramley and R. J. W. Le Fèvre
Reaction of L-threitol with acetone. By A. B. Foster, A. H. Olavesen, and J. M. Webber
2-Amino-2-imidazolines and 2-amino-2-oxazolines. By B. Adcock, Alexander Lawson, and D. H. Miles
Experiments confirming to the structure of shellolic acid. By W. Carruthers, J. W. Cook, (Mrs.) N. A. Glen (née McGinnis), and F. D. Gunstone
Quinazolines. Part III. The structure of the hydrated quinazoline cation. By Adrien Albert, W. L. F. Armarego, and E. Spinner.
1,2,3,4-Tetrahydroxy-1,4-dihydroxy-2-oxoquinolines: preparation by reductive cyclisations with hydrazine hydrate and palladium–charcoal. By. R. T. Coutts, M. Hooper, and D. G. Wibberley
Isatogens. Part I. Base-catalysed condensation products of methyl, and ethyl *o*-nitrobenzoylacetates, and *o*-nitrobenzoylacetone. By R. T. Coutts, M. Hooper, and D. G. Wibberley
Diterpenoid bitter principles. Part III. The constitution of clerodin. By D. H. R. Barton, H. T. Cheung, A. D. Cross, L. M. Jackman, and M. Martin-Smith
π-Molecular complex of hexamethylborazole with tetracyanoethylene. By N. G. S. Champion, R. Foster, and R. K. Mackie
The abnormal hydrolysis of certain β-(diarylphosphine) propionic esters. By Roy C. Hinton, Frederick G. Mann, and David Todd
The search for chemotherapeutic amidines. Part XIX. 3,3′-Diamidinocarbanilide and its congeners. By S. S. Berg
Reactions of sodium 2-oxocyclohexyl thiolsulphate. By Brian Milligan and J. M. Swan
Synthesis of (±)-cis-9-hydroxyoctadec-12-enoic acid. By J. Kennedy, A. Lewis, N. J. McCorkindale, and R. A. Raphael
Aromatic reactivity. Part XXI. Effects of strongly-deactivating substituents in protodetriethylgermylation. By C. Eaborn and K. C. Pande

XUM

841. *Complexes of Transition Metals with a Tetra-tertiary Arsine.*

By G. A. Barclay and A. K. Barnard.

The tetra-tertiary arsine $As(CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}AsMe_2)_3$ has been synthesised, and its complexes with salts of iron(II), iron(III), cobalt(III), nickel(II), and nickel(III) have been studied. The magnetic moments of these compounds indicate that in all cases the metal atom is spin-paired. The derivatives of the bivalent metals are six-covalent non-electrolytes of the type $[M\ ttaX_2]$; the tervalent derivatives are salts $[M\ ttaX_2]Y$ (tta = tetra-tertiary arsine).

The instability of the cobalt(II) and nickel(II) compounds is noteworthy.

In a previous paper we described cobalt complexes with a terdentate amine, 2,2′-diaminodiethylamine, and with a quadridentate amine, 2,2′,2″-triaminotriethylamine.[1] The complexes with the terdentate ligand have been compared with the corresponding derivatives of a tritertiary arsine $Me{\cdot}As(CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}AsMe)_2$.[2] The present paper describes the preparation of a tetra-tertiary arsine, tris-(3-dimethylarsinylpropyl)arsine, $As(CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}AsMe_2)_3$, and some of its metallic derivatives.

The tetra-tertiary arsine has four arsenic atoms available for co-ordination to the same metal atom. Models show that the arsine should be able to co-ordinate readily if the metal uses tetrahedral or octahedral bonding orbitals, but not if the bonds are square-planar.

Ligand-field theory indicates that when a metal in the latter half of the first transition series forms complexes with highly polarisable ligands (*e.g.*, tertiary arsines) then electron-pairing should occur in the $3d_\epsilon$-orbitals, giving the non-bonding configurations shown in Table 1. Consequently, for iron(II), iron(III), cobalt(III), and nickel(IV), where the $3d_\gamma$-

Table 1.

Metal and valency	Config.	No. of unpaired electrons	Metal and valency	Config.	No. of unpaired electrons
Iron(II)	$(3d_\epsilon)^6$	0	Nickel(II)	$(3d_\epsilon)^6(3d_\gamma)^2$	0 *
Iron(III)	$(3d_\epsilon)^5$	1	Nickel(III)	$(3d_\epsilon)^6(3d_\gamma)^1$	1
Cobalt(II)	$(3d_\epsilon)^6(3d_\gamma)^1$	1	Nickel(IV)	$(3d_\epsilon)^6$	0
Cobalt(III)	$(3d_\epsilon)^6$	0			

* See text.

orbitals are not occupied by non-bonding electrons, regular octahedral derivatives would be expected. However, in cobalt(II), nickel(II), and nickel(III), the $3d_\gamma$-orbitals are occupied by one or two electrons. These electrons, which occupy the $3d_{z^2}$-orbital, will repel the ligands in the *trans*-positions. The resultant stereochemistry will be either that of a distorted octahedron with two long *trans*-bonds, or, if the repulsion is sufficiently high, that of a square plane.[3] The $3d_{z^2}$-orbital will be in a fairly high ligand field compared with the $3d_\epsilon$-orbitals which point between the ligand directions. Consequently, electrons in the former orbital will be less firmly bound than the other non-bonding electrons and might be expected to be lost quite readily.

Summarising, it is predicted that the metal complexes of the tetra-arsine should be spin-paired and octahedral, and that the cobalt(II) and nickel(II) compounds should be fairly readily oxidised to the corresponding cobalt(III), and nickel(III) and nickel(IV) compounds.

The complexes of the tetra-arsine (tta) that we isolated, together with the complete magnetic data, are summarised in Table 2.

[1] Barclay and Barnard, *J.*, 1958, 2540.
[2] Barclay and Nyholm, *Chem. and Ind.*, 1953, 378; Barclay, *Rev. Pure Appl. Chem.* (*Australia*), 1954, **4**, 77.
[3] Orgel, "Introduction to Transition Metal Chemistry," Methuen, London, 1960, p. 63.

XUM

The ligand itself was synthesised by the reactions, $HO{\cdot}[CH_2]_3{\cdot}OH$ (+ S_2Cl_2) ⟶ $HO{\cdot}[CH_2]_3{\cdot}Cl$ (+ Na_2AsO_3) ⟶ $HO{\cdot}[CH_2]_3{\cdot}AsO_3H_2$ (+ SO_2 + HCl + $SOCl_2$) ⟶ $Cl{\cdot}[CH_2]_3{\cdot}AsCl_2$ (+ MeMgI) ⟶ $Cl{\cdot}[CH_2]_3{\cdot}AsMe_2$ (Grignard + $AsCl_3$) ⟶ As $([CH_2]_3{\cdot}AsMe_2)_3$. The product was a white wax, melting at ~23°, which, in contrast with simpler arsines, was not readily oxidised in air.

TABLE 2.

Magnetic susceptibilities of powdered samples at 20°.

Complex	Colour	$10^6\chi_M$	10^6D *	$10^6\chi'_M$	μ (B.M.)
Fe tta$(SCN)_2$	Purple	—†	—	—	0·0
Fe ttaCl_2 $FeCl_4$	Red	16,260	488	16,748	4·45
Co ttaCl_2 ClO_4	Green	—†	—	—	0·0
Co ttaBr_2 Br	Brown	—†	—	—	0·0
Co ttaBr_2 ClO_4	Brown	—†	—	—	0·0
Co ttaI_2 I	Brown	—†	—	—	0·0
Ni ttaI_2	Blue	—†	—	—	0·0
Ni ttaCl_2 ClO_4	Purple	1190	440	1630	1·96
Ni ttaBr_2 Br	Purple	1200	463	1663	1·98
Ni ttaBr_2 ClO_4	Blue	1150	461	1611	1·95
Ni ttaI_2 I	Green	1040	507	1597	1·94

* These values of the diamagnetic correction D are calculated from the constants given by Selwood [4]; the diamagnetism of the metal atom has been ignored in all cases.

† The method of measurement did not permit precise determination of diamagnetic susceptibilities.

The purple diamagnetic iron(II) compound Fe tta$(SCN)_2$ is a non-electrolyte in nitrobenzene. It can therefore be formulated as a spin-paired octahedral complex, with *cis*-thiocyanato-groups.

The complex Fe ttaCl_2,$FeCl_4$ has an effective magnetic moment of 4·45 B.M. per iron atom, intermediate between the values expected for three and four unpaired electrons. Nyholm [5] has pointed out that this situation may arise when a compound contains two metal atoms, one with a spin-free configuration, and the other spin-paired. Here, by analogy with the corresponding diarsine compound, it is probable that the anion is the tetrachloroferrate(III) ion. By subtracting the known susceptibility of this anion from the total, the susceptibility of the complex cation can be calculated:

	$10^6\chi_M$	10^6D	$10^6\chi'_M$	μ (B.M.)
Fe ttaCl_2 $FeCl_4$	16,260	488	16,748	4·45 per Fe
$[FeCl_4]^-$	15,060	94	15,154	5·98
$[Fe\ tta Cl_2]^+$	1200	394	1594	1·95

i.e., the cation is best formulated with a spin-paired octahedral configuration. This implies that the compound is a uni-univalent electrolyte, which is confirmed by the observed molar conductivity in nitrobenzene. Attempts to prepare the perchlorate salt of this cation led to decomposition.

In spite of numerous precautions to exclude oxidising agents, it was impossible to isolate a cobalt(II) complex. The cobalt(III) compounds are all diamagnetic uni-univalent electrolytes of the type $[Co\ tta X_2]Y$, a configuration supported by preparation of the dichloro- and the dibromo-perchlorate (X = Cl, Br; Y = ClO_4).

Similarly the complexes of nickel(II) proved difficult to prepare. In only one case, by using nickel iodide in an atmosphere of nitrogen, could such a compound be isolated. This dark blue di-iodide is diamagnetic and a non-electrolyte in nitrobenzene, and is formulated with a spin-paired octahedral configuration. The deeply coloured nickel(III) complex salts all have magnetic moments corresponding to one unpaired electron and are uni-univalent electrolytes in nitrobenzene. They are undoubtedly spin-paired octahedral

[4] Selwood, "Magnetochemistry," Interscience Publ., Inc., New York, 1956, 2nd edn., p. 91.
[5] Nyholm, *J.*, 1950, 851.

salts of the type [Ni ttaX$_2$]Y. This view is substantiated by isolation of the perchlorates [Ni ttaX$_2$]ClO$_4$ (X = Cl, Br). Attempts to obtain Ni(IV) compounds, which should be possible by removal of the single electron in the $3d_{z^2}$-orbital of a nickel(III) atom, proved unsuccessful: the oxidising agents (dilute nitric acid, chlorine, or ceric sulphate) caused the decomposition of the complex. With 15N-nitric acid a deep red solution was obtained initially, but this rapidly decomposed to give the green solution characteristic of the nickel(II) ion.

Consequently, in all cases investigated, a spin-paired octahedral configuration is believed to occur. In each case there are four metal–arsenic bonds and two metal–halogen or metal–thiocyanate bonds in *cis*-positions. However, covalent bonding between a metal atom and a perchlorate ion would not be expected, owing to the very low polarisability of the latter, and a different type of tetra-arsine complex should therefore arise. When alcoholic solutions of nickel perchlorate and the tetra-arsine are mixed a bright purple precipitate separates immediately. A similar precipitate is also obtained when any nickel tetra-arsine complex is treated with dilute perchloric acid or aqueous sodium perchlorate. This compound is insoluble in all the common solvents, precluding conductivity and molecular-weight measurements. It is diamagnetic, and the metal is therefore presumably bivalent. Analyses show that the composition varies from preparation to preparation, the results not fitting any reasonable formulation. These facts make it likely that the compound is polymerised by the sharing of tetra-arsine groups between different nickel atoms, in such a way that each becomes octahedrally co-ordinated by six arsenic atoms. It is interesting that Barclay and Nyholm [2] could not obtain a pure complex of nickel perchlorate with the tri-tertiary arsine. They attributed this to partial oxidation, but an alternative explanation is that the compound is polymeric, similarly to the tetra-arsine complex.

Experimental

Tris-(3,3′,3″-dimethylarsinylpropyl)arsine (" *tetra-arsine* ").—This preparation took place in a number of stages. First, trimethylene chlorohydrin was converted into dichloro-3-chloropropylarsine by the methods of Gough and King; [6] then 3-chloropropyldimethylarsine was prepared in the following manner: [7] A Grignard reagent, from methyl iodide (142 g.) and magnesium (24 g.), was filtered through glass wool and added slowly to a solution of dichloro-3-chloropropylarsine (100 g.) in dry ether (250 ml.). The whole was agitated by a stream of dry nitrogen during the addition and all subsequent operations. A vigorous reaction occurred, and initially a yellow solid separated, but eventually most of this disappeared, two layers being formed. After the final addition the mixture was refluxed for 10 min. and the complex decomposed by addition of ammonium chloride solution. The ethereal layer was separated and washed successively with water, saturated sodium hydrogen carbonate solution, and again with water. After drying (MgSO$_4$), the ether was removed and the residue distilled under reduced pressure in an atmosphere of coal gas. 3-Chloropropyldimethylarsine (65 g.), b. p. 60—62°/10 mm., was obtained as a colourless oil with a garlic odour.

Magnesium (10 g.) was covered with dry ether and a Grignard reaction started with a little methyl iodide. When the reaction was proceeding vigorously, 3-chloropropyldimethylarsine (65 g.) in dry ether (150 ml.) was added at such a rate as to keep the ether boiling. Then the mixture was refluxed for 15 min., cooled, and decanted through glass wool to remove the excess of magnesium, and arsenic trichloride (22 g.) in ether (60 ml.) was slowly added. Large quantities of a yellow solid were formed. The mixture was refluxed for 30 min., then the complex was decomposed with ammonium chloride solution, and the ethereal layer was separated, washed with sodium hydroxide solution and water, and dried (MgSO$_4$). The ether was distilled off and the remaining oil heated at 120°/3—4 mm. until all volatile matter was removed. The residue was cooled in solid carbon dioxide–alcohol, the *tetra-arsine* separating as a greasy white solid, m. p. ~23°. It was recrystallised from methanol (Found: C, 34·85; H, 7·05. C$_{15}$H$_{36}$As$_4$ requires C, 34·9; H, 7·05%).

[6] Gough and King, *J.*, 1928, 2439.
[7] Barclay and Nyholm, unpublished observations.

XUM

Dithiocyanato(tetra-arsine)iron(II).—Anhydrous ferric chloride (0·15 g.) was dissolved in ethanol (10 ml.), and the solution filtered, and treated with ammonium thiocyanate (0·28 g.) in ethanol (10 ml.). Tetra-arsine (0·5 g.) in warm ethanol (10 ml.) was added to the deep red solution. A dark brown precipitate rapidly separated and was set aside for 5 min. before collection. The filtrate was left overnight, small deep purple crystals being produced. This *complex* (0·3 g.) was recrystallised from ethanol (Found: C, 29·8; H, 5·35; Fe, 8·3. $C_{17}H_{36}As_4FeN_2S_2$ requires C, 29·65; H, 5·3; Fe, 8·1%); it had molecular conductivity ($9·3 \times 10^{-4}$M-solution in nitrobenzene) at 20° = 2·5 mho.

Dichloro(tetra-arsine)iron(III) *Tetrachloroferrate*(III).—Anhydrous ferric chloride (0·15 g.) was dissolved in ethanol (10 ml.), filtered, and added with vigorous stirring to a solution of tetra-arsine (0·5 g.) in ethanol (10 ml.). A brick-red precipitate was immediately formed and after 5 min. was filtered off and washed with ethanol in which it was only slightly soluble. The *complex* (0·4 g.) was dried in a vacuum-desiccator (Found: C, 21·6; H, 4·2; Fe, 13·2. $C_{15}H_{36}As_4Cl_6Fe_2$ requires C, 21·45; H, 4·3; Fe, 13·3%). Its molecular conductivity in $1·65 \times 10^{-3}$M-solution in nitrobenzene at 20° was 19·0 mho.

Dichloro(tetra-arsine)cobalt(III) *Perchlorate*.—Ethanolic solutions containing cobalt chloride hexahydrate (0·5 g.) and sodium perchlorate (0·35 g.) were mixed, filtered, and added to a solution of tetra-arsine (1·1 g.) in warm ethanol (20 ml.). The blue solution became deep red and an olive-green precipitate was produced. The *perchlorate* (0·6 g.) was filtered off and dried in a vacuum-desiccator [Found: C, 23·9; H, 4·8; Cl (not perchlorate), 9·6. $C_{15}H_{36}As_4Cl_3CoO_4$ requires C, 24·15; H, 4·9; Cl (not perchlorate), 9·6%]. The molecular conductivity in $2·6 \times 10^{-3}$M-solution in nitrobenzene at 20° was 25·0 mho.

Dibromo(tetra-arsine)cobalt(III) *Bromide*.—Cobalt bromide hexahydrate (0·3 g.) and lithium bromide (0·1 g.) in alcohol were mixed and added to a warm alcoholic solution of the tetra-arsine (0·45 g.). The brown solution was evaporated to dryness at room temperature. The complex was extracted from the excess of lithium bromide with chloroform, and this solution was treated at the b. p. with high-boiling light petroleum. On cooling, dark brown needles of the *bromide* (0·4 g.) were obtained (Found: C, 22·0; H, 4·4; Br, 29·4. $C_{15}H_{36}As_4Br_2Co$ requires C, 22·1; H, 4·45; Br, 29·4%); the molecular conductivity in $1·6 \times 10^{-3}$M-solution in nitrobenzene at 20° was 22 mho.

Dibromo(tetra-arsine)cobalt(III) *Perchlorate*.—Alcoholic solutions of cobalt bromide hexahydrate (0·7 g.) and sodium perchlorate (0·3 g.) were mixed, filtered, and added to a warm alcoholic solution of the tetra-arsine (1·0 g.). A khaki-brown precipitate of the *perchlorate* (0·7 g.) was rapidly produced (Found: C, 21·3; H, 4·2; Br, 19·1. $C_{15}H_{36}As_4Br_2ClCoO_4$ requires C, 21·6; H, 4·2; Br, 19·1%). The molecular conductivity in $1·4 \times 10^{-3}$M-solution in nitrobenzene at 20° was 21 mho.

Di-iodo(tetra-arsine)cobalt(III) *Iodide*.—Cobalt chloride hexahydrate (0·2 g.) and lithium iodide (0·8 g.) in alcohol were mixed and added to a warm alcoholic solution of the tetra-arsine (0·4 g.). On evaporation of the red-brown solution a deep-brown oil was obtained. This crystallised from chloroform–light petroleum, giving the dark brown *iodide* (0·4 g.) (Found: C, 18·7; H, 3·5; I, 39·75. $C_{15}H_{36}As_4CoI_2$ requires C, 18·8; H, 3·8; I, 39·9%), whose molecular conductivity in $1·3 \times 10^{-3}$M-solution in nitrobenzene at 20° was 23 mho.

Di-iodo(tetra-arsine)nickel(II).—A solution of nickel iodide (0·3 g.) in alcohol was boiled free from dissolved air and saturated with coal gas. The tetra-arsine (0·5 g.) in air-free alcohol was rapidly added and the deep blue solution vigorously shaken. It was concentrated in a vacuum-desiccator and filtered in an atmosphere of coal gas. Deep blue crystals of the *complex* (0·4 g.) were obtained (Found: C, 21·6; H, 4·5; Ni, 7·0. $C_{15}H_{36}As_4I_2Ni$ requires C, 21·75; H, 4·4; Ni, 7·1%), whose molecular conductivity in $1·4 \times 10^{-3}$M-solution in nitrobenzene at 20° was 5·1 mho.

Dichloro(tetra-arsine)nickel(III) *Perchlorate*.—This compound was prepared after attempts to isolate the trichloride had yielded only deep blue oils. Nickel chloride hexahydrate (0·2 g.) and sodium perchlorate (0·13 g.) in alcohol were mixed and added to a warm alcoholic solution of the tetra-arsine (0·45 g.). The deep blue solution, which almost immediately began to deposit purple crystals, was set aside overnight. The deep purple *perchlorate* (0·5 g.) was filtered off and dried in a vacuum-desiccator [Found: C, 23·9; H, 4·7; Cl (not perchlorate), 9·7; Ni, 7·8. $C_{15}H_{36}As_4Cl_3NiO_4$ requires C, 24·2; H, 4·9; Cl (not perchlorate), 9·6; Ni, 7·9%]. The molecular conductivity in $2·0 \times 10^{-3}$M-solution in nitrobenzene at 20° was 25·0 mho.

Dibromo(tetra-arsine)nickel(III) *Bromide*.—The tetra-arsine (0·8 g.) in warm alcohol was added to a filtered alcoholic solution containing nickel chloride hexahydrate (0·4 g.) and lithium

bromide (1·0 g.). The deep blue solution was evaporated at room temperature to a blue oil which crystallised from chloroform–light petroleum, giving the dark purple *bromide* (0·35 g.) (Found: C, 22·1; H, 4·35; Br, 29·5; Ni, 7·1. $C_{15}H_{36}As_4Br_2Ni$ requires C, 22·15; H, 4·5; Br, 29·45; Ni, 7·2%). The molecular conductivity in $1·6 \times 10^{-3}$M-solution in nitrobenzene at 20° was 25·0 mho.

Dibromo(tetra-arsine)nickel(III) *Perchlorate.*—A filtered alcoholic solution containing nickel bromide trihydrate (0·15 g.) and sodium perchlorate (0·07 g.) was added to a warm alcoholic solution of the tetra-arsine (0·26 g.). Deep blue crystals of the *perchlorate* (0·4 g.) were rapidly formed (Found: C, 21·8; H, 4·5; Br, 19·0; Ni, 6·9. $C_{15}H_{36}As_4Br_2ClNiO_4$ requires C, 21·6; H, 4·35; Br, 19·35; Ni, 7·0%). The molecular conductivity in $9·1 \times 10^{-4}$M-solution in nitrobenzene at 20° was 29·0 mho.

Di-iodo(tetra-arsine)nickel(III) *Iodide.*—The tetra-arsine (0·6 g.) in warm alcohol was added to a filtered alcoholic solution containing nickel chloride hexahydrate (0·3 g.) and lithium iodide (1·2 g.). The deep green solution was concentrated under reduced pressure, very dark green crystals of the *iodide* (0·3 g.) being obtained (Found: C, 18·7; H, 3·6; I, 39·8; Ni, 6·2. $C_{15}H_{36}As_4I_2Ni$ requires C, 18·8; H, 3·8; I, 39·9; Ni, 6·1%). The molecular conductivity in $1·6 \times 10^{-3}$M-solution in nitrobenzene at 20° was 25·0 mho.

Magnetic Measurements.—The magnetic susceptibilities were determined for the finely powdered solids (*ca.* 10 mg.) in an apparatus of the type described by Blaha.[8]

Conductivity Measurements.—A conductance bridge with a dip-type cell was used. It has been shown [9] that the molar conductivity of a uni-univalent electrolyte in nitrobenzene solution at room temperature is about 20—25 mho.

We thank the University of Leeds for the award of an I.C.I. Fellowship (to G. A. B.), and the D.S.I.R. for a maintenance grant (to A. K. B.). We are indebted to Professor E. G. Cox for his interest.

Department of Inorganic and Structural Chemistry,
The University, Leeds, 2.
[Present addresses: (G. A. B.) School of Chemistry, University of New South Wales, Broadway, Sydney, Australia.
(A. K. B.) Department of Science, Hatfield College of Technology, Hatfield, Herts. [*Received, March 1st,* 1961.]

[8] Blaha, *Mikrochem.*, 1952, **39**, 339.
[9] Ali, Brewer, Chadwick, and Garton, *J. Inorg. Nuclear Chem.*, 1959, **9**, 130, and references therein.

---

842. *The Electron-spin Resonance Spectra and Odd-electron Distribution of a Number of Polycyclic Semiquinones and Their Derivatives.*

By R. W. Brandon and E. A. C. Lucken.

The electron resonance spectra of *p*-benzosemiquinone, 1,4-naphthasemiquinone, 9,10-anthrasemiquinone, 9,10-phenanthrasemiquinone, 1,2-acenaphthasemiquinone, and of some of their alkyl, chloro-, and nitro-derivatives have been measured on an *X*-band spectrometer. It has thus been possible to assign unambiguously the measured splitting constants to the different protons of the parent semiquinones. Odd-electron densities in these compounds have been calculated by the L.C.A.O.-M.O. method and the splittings in the three *para*-semiquinones explained in terms of a unique pair of values for the coulomb integral of the oxygen atom and the carbon–oxygen resonance integral, $\alpha_O = \alpha_C + 0·39\beta_{C-C}$, $\beta_{C-O} = 1·06\beta_{C-C}$. The results for the *ortho*-semiquinones are explained with a variety of pairs of values for α_O and β_{C-O}, none of which however, corresponded to the *para*-semiquinone parameters.

Values of proton hyperfine splitting constants in electron-spin resonance spectra of conjugated organic radicals provide, in principle, a measure of the π-electron spin density

at the proton-bearing carbon atoms of the conjugated system.[1] A sensitive method is thus afforded for testing theoretical predictions of π-electron distribution, and Weissman and de Boer [2] have used it to show that the π-electron distribution in aromatic negative ions agrees well with that calculated by the simple Hückel molecular-orbital method. It has also been shown to account qualitatively for the spectra of *ortho*- and *para*-benzosemiquinones,[1] but here there arises the difficulty that values must be guessed for the oxygen coulomb integral, α_O, and the carbon–oxygen resonance integral, β_{C-O}, and that for any choice of coulomb integral it is usually possible to obtain satisfactory agreement with experiment by an appropriate choice of resonance integral.

It therefore seemed to us worth while to measure the electron-spin resonance spectra of a number of polycyclic semiquinones to see if the results could be explained in terms of a unique pair of parameters α_O and β_{C-O}. We have confirmed previous results on 1,4-naphthasemiquinone,[3] 9,10-anthrasemiquinone,[4] 9,10-phenanthrasemiquinone,[4] and acenaphthenesemiquinone,[4] and have measured the electron-spin resonance spectra of a number of their derivatives; thereby we have been able to assign splitting constants to the different protons in the parent compounds with reasonable certainty.

Experimental

1. *Preparation of the Semiquinones.*—The starting materials were the corresponding quinones. With the following exceptions they were commercially available: 2-Chloro-1,4-naphthaquinone was prepared by oxidation of 2-chloronaphthalene supplied by Dr. P. M. G. Bavin (formerly of this College); 2- and 4-nitro- and 2- and 3-chloro-phenanthraquinone by oxidation of the substituted hydrocarbons (2- and 3-chloro-phenanthrene were prepared by the method of Bachmann and Boatner [5] from the corresponding amines which were supplied by Dr. E. W. T. Warford, formerly of this College, who also supplied the two nitrophenanthrenes). An attempt was made to prepare 5,8-dichloro-1,4-naphthaquinone by oxidation of 1,4-dichloronaphthalene: the electron-spin resonance spectrum of the derived semiquinone showed however that the product was probably 4-chloro-1,2-naphthaquinone. Oxidations were carried out by slowly adding a solution of chromic oxide in acetic acid to one of the hydrocarbon in glacial acetic acid at 100°; the mixture was then poured into water; the precipitated quinone was filtered off, washed with dilute sodium hydroxide and water, and used for preparation of the semiquinone without purification.

The semiquinones were prepared from the corresponding quinones by one or both of the following methods.

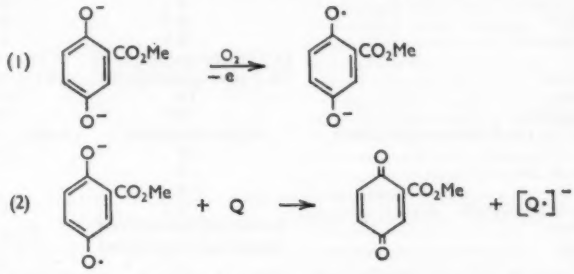
(*a*) To a $\sim 10^{-2}$M-solution of the quinone in ethanol two drops of concentrated alcoholic potassium hydroxide were added, with immediate formation of semiquinone radical-ions. The reaction is presumably oxidation of the alkoxide ion to the peroxide radical although it does not seem to have been previously reported. The nature of the alkoxide ion does not seem to be important, the systems methanol–sodium methoxide and t-butyl alcohol–potassium t-butoxide seeming to be equally efficient.

(*b*) In a number of cases, *e.g.*, 1,4,5,8-tetrachloroanthraquinone, the above reaction failed to produce semiquinones. The following method produced semiquinones in every case. Methyl quinol-2-carboxylate is autoxidised very rapidly in alkaline solution, the half-life of the intermediate semiquinone being a few minutes. To a solution in ethanol ($\sim 10^{-2}$-M each in the above quinol, and the quinone under study) were added 2 drops of concentrated alcoholic potassium hydroxide. The spectrum of the ester semiquinone at once appeared, then rapidly decayed and was replaced by that of the desired semiquinone. The sequence of reactions is presumably as annexed. It may be that the oxidising agent in stage (1) is the quinone, Q, itself. It is possible to substitute quinol for the quinol ester, but the unwanted benzosemiquinone radical disappears much more slowly.

[1] McConnel, *J. Chem. Phys.*, 1956, **24**, 764.
[2] Weissman and de Boer, *J. Amer. Chem. Soc.*, 1958, **80**, 4549.
[3] Wertz and Vivo, *J. Chem. Phys.*, 1956, **24**, 479.
[4] Adams, Blois, and Sands, *J. Chem. Phys.*, 1958, **28**, 774.
[5] Bachmann and Boatner, *J. Amer. Chem. Soc.*, 1936, **58**, 2194.

XUM

Measurement of Electron-spin Resonance Spectra.—The spectra were measured on an *X*-band spectrometer, constructed in this laboratory, having a H_{012} rectangular sample-cavity in one arm of a magic-tee bridge and employing 470 kc./sec. field modulation and phase-sensitive detection to increase sensitivity. A "Clarendon" electromagnet, supplied by Newport



Instruments Ltd., with a 3 cm. gap and shimmed polefaces provided the main magnetic field. The current for the magnet was obtained from a bank of heavy-duty lead accumulators, and the field was swept by passing an electronically generated saw-tooth current through a pair of Helmholtz coils mounted on the pole-pieces. The sweep was calibrated daily against a solution of peroxyaminedisulphonate ion in water. The resolving power of the spectrometer was ~0·25 oersted.

The number of hyperfine components and the splitting constants of all the semiquinones measured are shown in Table 1. The spectra of selected quinones are shown in Fig. 1.

Calculations of Electron-distribution by the Hückel Method.—The standard assumptions of the Hückel method were made, *i.e.*, $\Psi_a = c_{oi}\psi_i$, where Ψ_a is a molecular orbital, c_{oi} is a numerical coefficient, and ψ_i is the $2p_z$-atomic orbital of atom "i" in the conjugated system. Application of the variation principle gives the secular determinant

$$|H_{ij} - ES_{ij}| = 0$$

where

$$H_{ij} = \int \psi_i H \psi_j^* \, d\tau$$

$$S_{ij} = \int \psi_i \psi_j^* \, d\tau,$$

H being an effective one-electron Hamiltonian operator for the system. Overlap was neglected, *i.e.*, $S_{ij} = \delta_{ij}$, where δ_{ij} is the Krönecker delta. All carbon atoms were supposed to have the same value of the coulomb integral H_{ii} ($\equiv\alpha$), and the resonance integral H_{ij} between neighbouring carbon atoms i and j was likewise presumed to be constant (β). Resonance integrals between non-neighbours were set equal to zero. The oxygen coulomb integral was given the value $\alpha + \rho\beta$ and the carbon–oxygen resonance integral the value $\gamma\beta$, where ρ and γ are parameters. ρ was allowed to take on values 0·0—1·4 inclusive and γ values 0·8—1·2 inclusive in steps of 0·1. The equations were solved by the courtesy of Imperial Chemical Industries Limited on their computer.

For this investigation it was supposed that the spin density was equal to the odd-electron density, *i.e.*,:

$$\Delta H_i = Q_p c_{oi}^2$$

where ΔH_i is the splitting produced by the proton on carbon atom "i," c_{oi} is the coefficient of ψ_i in the highest occupied orbital, *i.e.*, containing the odd electron, and Q_p is the proton splitting constant. This is now known to be incorrect, but probably not too important for the even-alternant systems considered here. De Boer and Weissman [2] were able with this assumption to explain the splitting constants of the different protons in a particular hydrocarbon radical-ion, but in order to compare different ions it was necessary to use a different value of Q_p for each molecule.

The results of these calculations are shown graphically in Figs. 2—7. The graphs are of two types: (*a*) The ratios of orbital coefficients of two different carbon atoms within the same molecule are plotted against the parameters ρ and γ; and (*b*) the ratio of a coefficient of one

XUM

TABLE 1.

Hyperfine components and splitting constants of semiquinones.

Semiquinone	No. of hyperfine components	Splitting constant(s) (oersted)
1,4-Benzo-	5 †	2·37 ± 0·04
2-Chloro-1,4-benzo- [a]	4 †	2·27 ± 0·04
2,6-Dimethyl-1,4-benzo- [a]	9 †	2·13 ± 0·04
1,4-Naphtha- [b]	15 † (three quintuplets)	3·19 ± 0·4; 0·58 ± 0·04
2-Methyl-1,4-naphtha- [b]	25 † (five quintuplets)	3·31 ± 0·04; 0·66 ± 0·04
2-Chloro-1,4-naphtha-	10	0·66 ± 0·4
2,3-Dichloro-1,4-naphtha-	5 †	0·65 ± 0·04
[Oxidation product of 1,4-dichloronaphthalene	4 (two doublets)	0·86 ± 0·4; 0·62 ± 0·04]
9,10-Anthra- [c]	13	0·58 ± 0·04
1-Chloro-9,10-anthra-	>8	~0·7
2-Chloro-9,10-anthra-	>8	~0·7
1,4,5,8-Tetrachloro-9,10-anthra-	5 †	1·13 ± 0.04
2-Methyl-9,10-anthra-	Broad and unresolved	Line width ~2·8
2-Ethyl-9,10-anthra-	Broad and unresolved	Line width ~2·6
9,10-Phenanthra- [c]	5 †	1·66 ± 0·1
2-Nitro-9,10-phenanthra-	5 †	1·60 ± 0·1
4-Nitro-9,10-phenanthra-	5 †	1·65 ± 0·1
2-Chloro-9,10-phenanthra-	5 †	1·58 ± 0·1
3-Chloro-9,10-phenanthra-	4 †	1·60 ± 0·1
3-Isobutyl-9,10-phenanthra-	4 †	1·52 ± 0·1
3-Acetyl-9,10-phenanthra-	4 †	1·33 ± 0·1
3-Cyclohexyl-9,10-phenanthra-	4 † (traces of fine structure)	1·65 ± 0·1
1,2-Acenaphtha- [c]	5 †	1·30 ± 0·04

[a] See also ref. 6. [b] See also ref. 3. [c] See also ref. 4.

† The intensity ratio of the lines of the multiplet are approximately proportional to the coefficients of a in the binomial expansion of $(1 + a)^{n-1}$ where n is the number of lines.

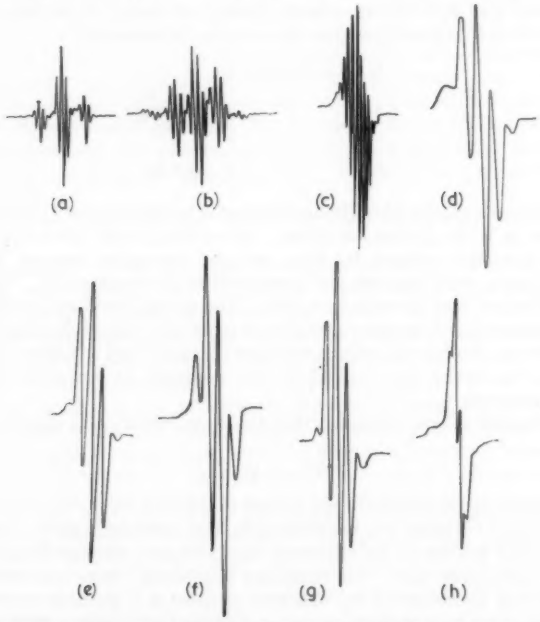


FIG. 1. Electron-spin resonance spectra of semiquinones, from (a) 1,4-naphthaquinone, (b) 2-methyl-1,4-naphthaquinone, (c) anthraquinone, (d) phenanthraquinone, (e) 2-chlorophenanthraquinone, (f) 3-chlorophenanthraquinone, and (g) 4-nitrophenanthraquinone, and from (h) the oxidation product from 1,4-dichloronaphthalene.

[c] Venkataraman, Segal, and Fraenkel, *J. Chem. Phys.*, 1959, **30**, 1006.

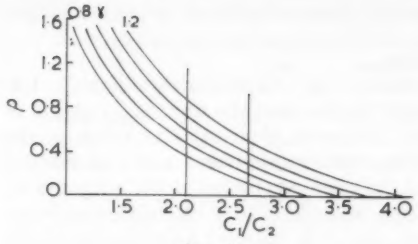


FIG. 2.

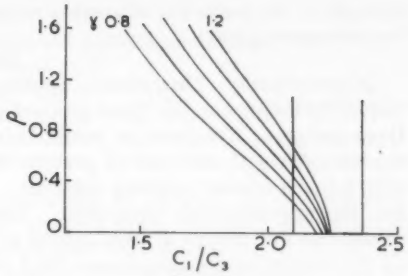


FIG. 3.

FIGS. 2 and 3. Ratios of orbital coefficients for (Fig. 2) $C_{(1)}$ and $C_{(2)}$, and (Fig. 3) $C_{(1)}$ and $C_{(3)}$ of 1,4-naphthaquinone, plotted against the parameters ρ and γ.

Here, and in Figs. 4—7, successive plots for γ are at intervals of 0·1. Throughout, for naphthaquinone, C_1, C_2, and C_3 refer to positions 1(= 2), 5(= 8), and 6(= 7) respectively; other molecules are numbered as usual.

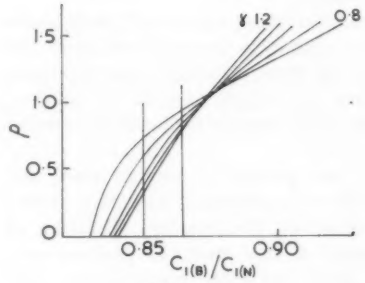


FIG. 4.

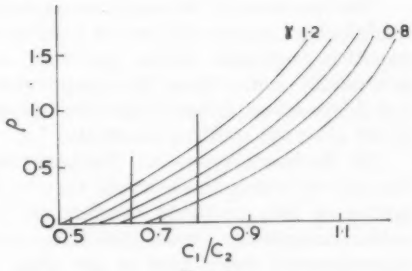


FIG. 5.

FIG. 4. Ratio of orbital coefficients of $C_{(1)}$ of 1,4-benzoquinone (C_{1B}) and 1,4-naphthaquinone (C_{1N}) plotted against the parameters ρ and γ.

FIG. 5. Ratio of orbital coefficients for $C_{(1)}$ and $C_{(2)}$ of 9,10-anthraquinone, plotted against the parameters ρ and γ.

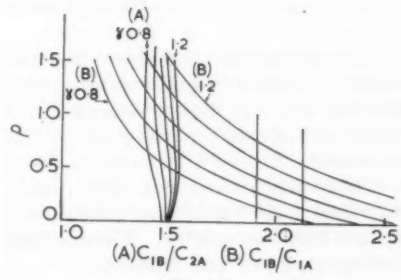


FIG. 6.

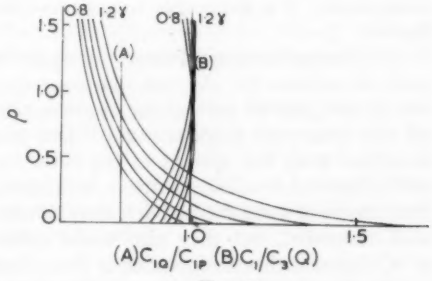


FIG. 7.

FIG. 6. Ratio of orbital coefficients for $C_{(1)}$ of 1,4-benzoquinone (C_B) and (A) $C_{(2)}$ and (B) $C_{(1)}$ of 9,10-anthraquinone (C_A) plotted against the parameters ρ and γ.

FIG. 7. Ratio of orbital coefficients for (A) $C_{(1)}$ of acenaphthaquinone (C_Q) and phenanthraquinone (C_P), and (B) $C_{(1)}$ and $C_{(3)}$ of acenaphthaquinone, plotted against the parameters ρ and γ.

XUM

molecule to the coefficient of another molecule, usually benzosemiquinone, is plotted against the parameters ρ and γ.

Discussion

Experimentally Determined Splitting Constants.—(a) *Naphthasemiquinones.* 1,4-Naphthasemiquinone has three pairs of equivalent protons and the spectrum consists of three groups of five lines, as would be expected if it arose from the interaction of the electron-spin with one pair of protons with a large splitting constant and four protons with a much smaller splitting constant. Two of the pairs of protons in the semiquinone are thus approximately equivalent. The spectrum of 2-methyl-1,4-naphthasemiquinone consists of five groups of overlapping quintuplets and it is known [6] from measurements on the methylbenzosemiquinones that the splitting produced by a proton in a methyl group attached to a conjugated carbon atom is approximately the same as would be produced by a proton directly attached to the same atom. These spectra are then at once explicable if we assume that in naphthasemiquinone the larger splitting constant is due to protons 2 and 3 while the smaller constant is due to the set 5, 6, 7, and 8. Had protons 2 and 3 belonged to the set giving the smaller constant, the spectrum of the 2-methyl derivative would have consisted of three overlapping groups of seven lines. This conclusion is wholly confirmed by the five-line spectrum of 2,3-dichloro-1,4-naphthasemiquinone and the ten-line spectrum of the 2-chloro-derivative.

The spectrum of the semiquinone derived from the oxidation product of 1,4-dichloronaphthalene consists of a pair of doublets and therefore cannot be due to 5,8-dichloro-1,4-naphthasemiquinone whose spectrum would consist of three triplets. The splitting presumably comes from two inequivalent protons and it is suggested that the product is 4-chloro-1,2-naphthaquinone, the 3-proton giving the larger and the 8-proton the smaller of the observed splitting constants.

(b) *Anthrasemiquinones.* Anthrasemiquinone has two groups of four protons, and the derived semiquinone would thus be expected to have a spectrum consisting of five groups of five, probably overlapping, lines. The observed thirteen-line spectrum of anthrasemiquinone would arise if the splitting constant of one group of protons were approximately twice that of the other group, *i.e.*, 1·16 and 0·58, respectively. The spectrum of 1,4,5,8-tetrachloroanthrasemiquinone strongly supports this interpretation, the observed splitting of 1·13 oersted being almost exactly twice that in the unsubstituted compound, and shows moreover that the 2-, 5-, 6-, and 7-protons are responsible for the larger of the splitting constants. The spectra of the remaining four anthrasemiquinone derivatives are not well resolved; in particular the spectra of the chloro-derivatives suffer from the relaxation time asymmetry noted by Ebsworth and Weil [7] for peroxydicobalt compounds; it is impossible to say more than that they do not contradict the hypothesis above.

(c) *Phenanthrasemiquinones.* Despite the fact that phenanthrasemiquinone has four pairs of protons the electron-spin resonance spectrum is relatively simple, showing that two of the pairs of protons are approximately equivalent and that the splitting produced by the other two pairs is small. The protons responsible for the splitting are readily identified from the spectra of the substituted compounds. 2- and 4-Substituted derivatives have a five-line spectrum resembling that of 9,10-phenanthrasemiquinone, while the spectra of 3-substituted derivatives have only four lines. No 1-substituted derivatives were measured, but they also would presumably have four-line spectra. The splitting in 9,10-phenanthrasemiquinone is thus attributed to the 1-, 3-, 6-, and 8-protons.

(d) *Acenaphthasemiquinone.* The spectrum of this compound resembles that of 9,10-phenanthrasemiquinone, consisting of five lines. No derivatives of acenaphthaquinone were measured and the results of the molecular-orbital calculations must be anticipated in assigning the splitting to the 1-, 3-, 4-, and 6-protons. The splitting due to the 2- and 5-protons is expected to be small, in agreement with the observed spectrum.

[7] Ebsworth and Weil, *J. Phys. Chem.*, 1959, **63**, 1890.

XUM

TABLE 2.

Ratios of splitting constants of benzosemiquinone, naphthasemiquinone, and anthrasemiquinone.

Semiquinone	ΔH_1	ΔH_2, ΔH_3	$\frac{\Delta H_1}{\Delta H_2}$; $\frac{\Delta H_1}{\Delta H_3}$	$\sqrt{\frac{\Delta H_1}{\Delta H_2}}$	$\sqrt{\frac{\Delta H_{\text{Benzosemiquinone}}}{\Delta H_1}}$
1,4-Naphtha-	3·19 (±0·04)	0·45—0·71	7·08—4·4	2·66—2·10	0·865—0·850
9,10-Anthra-	0·52—0·64	1·28—1·04	0·406—0·615	0·637—0·784	2·13—1·92

The results of the foregoing discussion are summarised in Table 2. If it is assumed that the resolution of the spectrometer is 0·25 oersted, then, provided the splitting constants of two protons in a molecule differ by less than 0·25 oersted, they will not be differentiated in the spectrometer. The same applies to two non-equivalent pairs of protons, which means that the splitting constants of the (6,7)- and (5,8)-protons may lie anywhere in the region 0·45—0·71 oersted, the average of the two constants being equal to the observed 0·58 oersted. A similar argument leads to the conclusion that the splitting constant (ΔH_1) of the (1,4,5,8)-protons in anthrasemiquinone lies between 0·52

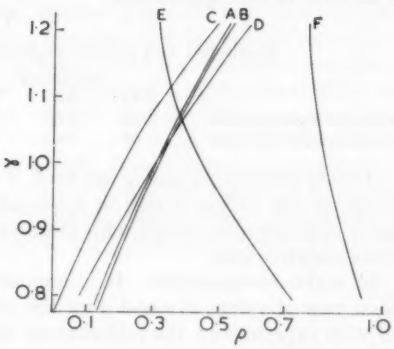


FIG. 8. Plots of ρ against γ (for connotation of A—F see text).

and 0·64 oersted, and that of the (2,3,6,7)-protons (ΔH_2) between 1·04 and 1·28 oersted in the weighted mean of the splitting constants, the value of $(2\Delta H_1 + \Delta H_2)/2$ being 1·16 oersteds. On this basis the limits of the mutual ratios of the various constants corresponding to the ratios of the orbital coefficients plotted in Figs. 2—7 are shown in Table 2. Since the ratio of the orbital coefficients should be equal to the square root of the ratio of the splitting constants, these are also given and correspond to the pairs of vertical lines plotted in Figs. 2—7.

Molecular-orbital Calculations.—The approximations involved in the theory make it likely that different parameters will be necessary for *ortho*- and *para*-semiquinones and therefore these are considered separately.

(a) para-*Semiquinones.* Consideration of Fig. 3 shows that if the Hückel theory has any value in this application, then ΔH_3 for naphthaquinone must lie in the upper quarter of its range of possible values, *i.e.*, $2{\cdot}10 < \sqrt{(\Delta H_1/\Delta H_3)} < 2{\cdot}25$ and hence $2{\cdot}45 < \sqrt{(\Delta H_1/\Delta H_2)} < 2{\cdot}66$. By trial and error it is found that, if $\sqrt{(\Delta H_1/\Delta H_3)} = 2{\cdot}15$ and hence $\sqrt{(\Delta H_1/\Delta H_2)} = 2{\cdot}61$, then two almost coincident curves relating ρ and γ are obtained from Figs. 2 and 3. These are shown in Fig. 8 as curves A and B. Any other choice of ΔH_2 and ΔH_3 produces two almost parallel curves.

Similar consideration of Figs. 5 and 6 for anthraquinone shows that only the choice of $\Delta H_1 = 0{\cdot}56$ (and hence $\Delta H_2 = 1{\cdot}20$) gives a pair of coincident curves relating ρ and γ, which also coincide with those derived from naphthasemiquinone. These are labelled C and D in Fig. 8.

The results thus far considered do not provide a unique pair of parameters ρ and γ. Fortunately, however, Fig. 4 produces a curve relating ρ and γ which crosses the previous

XUM

set. Unfortunately, the ratio $\sqrt{(\Delta H_B/\Delta H_1)}$ (where B denotes benzosemiquinone) for naphthalene is not very sensitive to ρ and γ, and the uncertainty in the experimental ratio $\sqrt{(\Delta H_B/\Delta H_1)}$ becomes very serious, the curves for the limiting ratios being shown as E and F in Fig. 8. Curve F, however, crosses A, B, C, and D at points where they are already diverging significantly from each other, while curve E crosses them in the region where they coincide the most (*i.e.*, $\rho = 0{\cdot}49$; $\gamma = 1{\cdot}06$). Rather laborious trial and error shows that no other values for the ratios of the splitting constants provide a unique pair of ρ and γ. In view of the approximation of equating spin-density and odd-electron density, this may not necessarily be an argument in favour of their adoption. They are, however, the best values obtainable within the scope of the present work. Since, however, this was completed, precise measurements by Vincow [8] of the splitting constants of the semiquinones discussed here have come to our attention. These are compared in Table 3 with our predictions from molecular orbital theory for the values $\rho = 0{\cdot}39$ and $\gamma = 1{\cdot}06$ derived from our less precise measurements, with ΔH for benzosemiquinone assumed as 2·37 oersteds. Agreement is remarkably good, demonstrating the general adequacy of our method in this application.

TABLE 3.

Predicted and precise experimental values of splitting currents.

	Predicted			Vincow's data		
	ΔH_1	ΔH_2	ΔH_3	ΔH_1	ΔH_2	ΔH_3
1,4-Naphthasemiquinone ...	3·28	0·62	0·50	3·23 ± 0·01	0·635 ± 0·005	0·513 ± 0·003
9,10-Anthrasemiquinone ...	0·56	1·01	—	0·55 ± 0·004	0·962 ± 0·005	—

If these values of ρ and γ are used, a value of 0·076 is obtained for the odd-electron density at the carbon atoms in 1,4-benzosemiquinone and hence Q_p equals 31 oersted. This is in reasonable accord with the range found by Weissman and de Boer for hydrocarbon negative ions.

(b) ortho-*Semiquinones*. It is impossible, from the data presented here, to derive a unique pair of values of ρ and γ for the *ortho*-semiquinones. Qualitatively, theory agrees well with experiment: the odd-electron densities at the (1,8)- and (3,6)-positions of 9,10-phenanthrasemiquinone are approximately equal and large; those at the (2,7)- and (4,5)-positions are always much smaller. Similarly the (2,7)- and (4,5)-odd-electron densities in acenaphthasemiquinone are always approximately the same (Fig. 7B) while the density at the (2,6)-positions is very small indeed. The ratio between the splitting constants for phenanthrasemiquinone and acenaphthasemiquinone (Fig. 7A) shows, as expected, that the values obtained for the *para*-quinones will not be suitable for *ortho*-semiquinones.

In sum, our results show that simple molecular-orbital theory suffices to explain the electron-spin resonance spectra of the semiquinones and that a unique pair of parameters, $\rho = 0{\cdot}39$ and $\gamma = 1{\cdot}06$, account for the observed spectra of *para*-semiquinones. Calculations are in progress to see whether allowing for the inductive effect of the oxygen atoms will produce a pair of parameters suitable for both *para*- and *ortho*-quinones and whether these are modified by calculations of actual spin-densities rather than odd-electron densities.

We thank the Central Research Fund of the University of London for a grant for purchase of equipment. One of us (R. W. B.) thanks the Department of Scientific and Industrial Research for a research award.

QUEEN MARY COLLEGE (UNIVERSITY OF LONDON),
MILE END ROAD, LONDON, E.1.
[Present addresses:
(R. W. B.) UNIVERSITY OF CHICAGO, CHICAGO, ILLINOIS, U.S.A.
(E. A. C. L.) CYANAMID EUROPEAN RESEARCH INSTITUTE, 91, ROUTE DE LA CAPITE, COLOGNY, GENEVA, SWITZERLAND.]
[*Received, March 27th*, 1961.]

[8] Vincow, *Diss. Abs.*, 1960, **20**, 3973.

843. *The Reactions of Hydroxyl Radicals with Hydrocarbons in Aqueous Solution.*

By T. Bérces and A. F. Trotman-Dickenson.

The relative reactivities of methane, ethane, propane, n-butane, isobutane, and cyclopropane with hydroxyl radicals produced by the photolysis of hydrogen peroxide and nitric acid have been determined by a method which depends on the study of the rate of consumption of two hydrocarbons. Incidentally the solubilities of the hydrocarbons in aqueous media have also been determined. Hydroxyl radicals in solution at 17·5° react in the same way as chlorine atoms in the gas phase at 25°.

Transfer reactions of hydroxyl radicals with most hydrocarbons, $\cdot OH + RH = H_2O + R\cdot$, are exothermic to the extent of 20 kcal. mole^{-1} or more. They might therefore be expected to have low activation energies, probably similar to those of reactions of chlorine or even fluorine atoms. The only studies of these reactions that have been reported are considered to be of doubtful reliability.[1] They indicate [2] that the activation energies are as high as 7—10 kcal. mole^{-1}. These high values are supported by the more reliable work on the reaction with hydrogen which has been studied directly and as a step in the hydrogen–oxygen reaction.[3,4]

The reactions have here been studied for the liquid phase because it was simpler to generate hydroxyl radicals in that medium than in the gas phase, although in all other ways this procedure introduced complications. Hydroxyl radicals were produced by the photolysis of both hydrogen peroxide and nitric acid: they then reacted with the mixture of dissolved hydrocarbons:

$$\cdot OH + R^1H = H_2O + R^{1}\cdot \quad \ldots\ldots\ldots\

Where the primes indicate that the units of the rate constants are a function of the dimensions of the system. From these equations we derive

$$\frac{k_1K_1}{k_2K_2} = \frac{\log (v_{r1})_i - \log (v_{r1})_f}{\log (v_{r2})_i - \log (v_{r2})_f}$$

Where the subscripts i and f indicate the initial and the final amounts of the reactants. It may be noted that because the absorption coefficients of hydrocarbons in aqueous solutions are very low, K_1/K_2 is nearly equal to α_1/α_2. Surprisingly, the solubilities of very few gaseous hydrocarbons in water have been reported; these had therefore to be determined.

Experimental

Materials.—The hydrocarbons were obtained from cylinders and degassed. The iodine, hydrogen peroxide, and perchloric and nitric acid were of " AnalaR " grade. Ordinary distilled water was used.

Determination of Rate Constants.—A quartz cylindrical reaction vessel (7 c.c.; 6 cm. long) was filled with a solution of hydrogen peroxide or nitric acid until an air-space of about 2 c.c. remained. This vessel terminated in a length of narrow quartz tubing and a ground joint. The vessel was attached to the vacuum system, then cooled in liquid nitrogen, and evacuated. After measured quantities of two hydrocarbons from a gas burette had been condensed on top of the solution the vessel was sealed and allowed to warm. The dead space was small, so that when methane was used the amount in the vessel could be accurately estimated.

The vessel was then attached to a Vibro shaker so that it was shaken horizontally, breaking the surface of a water bath through which tap water flowed. It was irradiated by the full light from a medium-pressure mercury arc for 1—2 hr. At the end of the run the vessel was marked with a file and placed in a rubber-and-glass tube. The tube was evacuated and the neck of the vessel broken. Several trials were required before a suitable device for opening the quartz vessel was found. In the early designs the containing tube was frequently broken by the vessel which was propelled by the stream of high-pressure gas surging out of it. All the liquid was distilled out of the vessel into two traps cooled in alcohol–solid carbon dioxide. The gases were collected in a trap (attached to the chromatography apparatus) which was cooled in liquid nitrogen. Several distillations of the aqueous mixture were needed to ensure that all the hydrocarbons were liberated. Control runs showed that the procedure was satisfactory. A special Toepler pump and a pump-down trap were used in handling methane.

The gases were analysed on a gas–solid chromatographic apparatus with a Janak nitrometer detector. The columns were of alumina (40—60 mesh), poisoned with 1·5% of squalane, except for the separation of methane which required an activated charcoal column.

Determination of Solubilities.—A suitable volume of a hydrocarbon, measured on a gas burette, was introduced into a vessel of known volume, placed in a thermostat bath and containing a known volume of liquid which was stirred. The pressure in the system was measured after sufficient time (1—2 hr.) for establishment of equilibrium. As the pressure was read before and after the introduction of the gas there was no need completely to degass the liquid. This simple procedure with a vessel of 784 c.c. filled with 684 c.c. of liquid yielded results that were reproducible to ±1%. The values found for Bunsen's absorption coefficient at 17·5° are:

Hydrocarbon	$10^4\alpha$ Water	$10^4\alpha$ 0·5N-HNO_3	Hydrocarbon	$10^4\alpha$ Water	$10^4\alpha$ 0·5N-HNO_3
Methane	416 ± 15	—	Cyclopropane	—	379 ± 1
Ethane	679 ± 5	648 ± 2	*n*-Butane	471 ± 5	—
Propane	543	534	Isobutane	355 ± 4	—

Results and Discussion

Table 1 lists results obtained with n-butane–propane mixtures when iodine and large quantities of oxygen were added to the system to remove alkyl radicals as they were formed. The additives do not alter the results. The results obtained for isobutane–propane (Table 2) with hydrogen peroxide [k(isobutane)/k(propane) = 1·02] and with

nitric acid (k ratio = 1·12) differ by little more than the experimental errors. A medium effect probably slightly alters the relative rates of identical reactions. Since no detailed studies of the photolysis of nitric acid have been reported, the similarity of the results with the peroxide and the acid are relied on as evidence that the acid splits into hydroxyl and nitrogen dioxide (which seems the most likely primary act). Hydroxyl radicals are known to be formed by photolysis of the peroxide [4] and are the only radicals that could also be formed from the acid. Some HO_2· must be formed by the reaction of hydroxyl

TABLE 1.

Reaction of hydroxyl radicals with n-butane–propane mixtures at 17·5°.

n-Butane (c.c. at N.T.P.)		Propane (c.c. at N.T.P.)		Medium		$\frac{k(\text{n-butane})}{k(\text{propane})}$
Initial	Final	Initial	Final	H_2O_2 (M)	$HClO_4$ (M)	
4·03	1·82	6·54	3·32	0·9	0·02 [a]	1·35
4·18	2·73	6·60	4·59	0·1	0·10 [a]	1·35
4·20	3·02	5·42	4·08	0·3	0·03 [a]	1·33
4·20	2·22	4·33	2·47	0·9	0·02 [b]	1·31
4·67	2·56	4·60	2·72	0·9	0·02	1·32
5·91	4·70	4·86	4·05	0·08	0·08 [a,b]	1·41
5·62	1·99	3·27	1·29	0·9	0·02 [a]	1·29
6·47	2·48	2·88	1·19	0·9	0·02 [a]	1·25

[a] In presence of 1 atm. of oxygen. [b] In presence of iodine.

TABLE 2.

Reaction of hydroxyl radicals with isobutane–propane mixtures at 17·5°.

Isobutane (c.c. at N.T.P.)		Propane (c.c. at N.T.P.)		Medium			$\frac{k(\text{isobutane})}{k(\text{propane})}$
Initial	Final	Initial	Final	H_2O_2 (M)	HNO_3 (M)	$HClO_4$ (M)	
2·85	2·02	6·47	3·86	0·6	—	0·07	1·03
6·13	5·58	6·20	5·36	0·2	—	0·02	1·00
6·56	4·84	6·56	4·06	0·6	—	0·07	1·00
5·93	4·30	5·92	3·57	0·6	—	0·07	0·98
6·64	5·89	3·01	2·51	0·2	—	0·02	1·06
6·29	4·27	2·84	1·59	0·6	—	0·07	1·03
						Mean =	1·02 ± 0·03
3·52	2·47	7·15	4·44	—	0·5	—	1·13
4·91	3·25	7·38	4·19	—	0·5	1	1·12
3·34	2·06	3·68	1·98	—	0·5	—	1·19
6·66	4·92	6·69	4·32	—	0·5	1	1·06
6·37	4·67	6·28	3·99	—	0·5	—	1·06
5·20	4·20	4·75	3·59	—	0·5	2	1·17
6·80	4·06	3·57	1·75	—	0·5	1	1·10
6·89	4·26	3·47	1·85	—	0·5	—	1·17
						Mean =	1·12 ± 0·06

TABLE 3.

Relative reactivities.

	Hydroxyl (17·5°, solution).	Chlorine atom (25°, gas)
Methane	0·42	0·0024
Ethane	1	1
Propane	2·78	2·71
Cyclopropane	0·18	0·0031
n-Butane	3·70	3·66
Isobutane	3·14	2·99

with the peroxide,[4] but as its reactivity is thought to be considerably lower than that of hydroxyl it should not affect the consumption of hydrocarbon.

If this conclusion is accepted, then Table 3, which shows the relative reactivities of the

XUM

hydrocarbons at 17·5°, shows our results with cyclopropane–methane–hydrogen peroxide, cyclopropane–propane–nitric acid, and propane–ethane–hydrogen peroxide.

The similarity of the relative reactivities of the alkanes, apart from methane, with the hydroxyl radicals and chlorine atoms is so marked that the absolute reactivities are probably also similar. This conclusion is supported by the general parallelism (Table 4) between high reactivity and low selectivity for small free radicals and by the way in which the present observations on hydroxyl fit the series.

The results indicate that the activation energies for the reactions of hydroxyl radicals with alkanes in aqueous solution are only 1—2 kcal. mole^{-1}. A hydroxyl radical is

TABLE 4.

Relative reactivities of hydrogen atoms in various environments with various radicals, $X\cdot + RH \longrightarrow XH + R\cdot$.

Radical, X·	Methyl	Cyclopropyl	CH_3	CH_2	CH	*E*	Ref.
F (25°)	0·8	0·9	1	1·2	1·4	0·3	*a*
OH (17·5°)	0·6	0·18	1	4·7	9·8	—	*b*
Cl (25°)	0·004	0·003	1	4·6	8·9	1·0	*c*
CF_3 (182°)	0·08	—	1	6	36	7·5	*d*
MeO (230°)	—	0·35	1	8	27	7·1	*e*
Me (182°)	0·04	0·55	1	7	50	11	*f*
Br (98°)	0·002	—	1	250	6300	13·4	*g*

E is the activation energy for the attack of the radical on ethane, in kcal. mole^{-1}.

Refs.: (*a*) Fettis, Knox, and Trotman-Dickenson, *J.*, 1960, 1064. (*b*) This work. (*c*) Knox and Nelson, *Trans. Faraday Soc.*, 1959, **55**, 937; Pritchard, Pyke, and Trotman-Dickenson, *J. Amer. Chem. Soc.*, 1955, **77**, 2629. (*d*) Ayscough, Polanyi, and Steacie, *Canad. J. Chem.*, 1955, **33**, 743; Ayscough and Steacie, *ibid.*, 1956, **34**, 103; Ayscough, *J. Chem. Phys.*, 1956, **24**, 944; Pritchard, Pritchard, Schiff, and Trotman-Dickenson, *Trans. Faraday Soc.*, 1956, **52**, 849. (*e*) Shaw and Trotman-Dickenson, *J.*, 1960, 3210; Bérces and Trotman-Dickenson, *J.*, 1961, 348. (*f*) Trotman-Dickenson, "Gas Kinetics," Butterworths, London, 1955. (*g*) Fettis, Knox, and Trotman-Dickenson, *J.*, 1960, 4177.

probably much more highly solvated than is the activated complex which it forms with an alkane. Therefore still greater reactivity would be expected in the gas phase. Russell [5] noted that solvated chlorine atoms were markedly more selective in their attack on hydrocarbons than were the atoms that reacted in the gas phase. More work will clearly be needed to resolve the disagreement between these results and those of Avramenko and his collaborators.

This work has been made possible through the support and sponsorship of the U.S. Department of Army, through its European Research Office.

EDINBURGH UNIVERSITY.
[Present address (A. F. T.-D.): EDWARD DAVIES CHEMICAL LABORATORY, ABERYSTWYTH.]
[*Received, March 20th*, 1961.]

[5] Russell, *J. Amer. Chem. Soc.*, 1957, **79**, 2977.

844. *Competitive Oxidations. Part III.*[1] *Oxidations at Low Temperatures Induced by Light.*

By W. E. Falconer, J. H. Knox, and A. F. Trotman-Dickenson.

The relative rates of consumption of alkanes by the attack of radicals generated by photolysis of ketones in the presence of an excess of oxygen have been determined. The relative reactivities of different C–H bonds towards these radicals, which are presumed to be alkylperoxy, have been estimated. The reactivities are the same as those found for the chain-carrying radicals in hydrocarbon oxidations at low temperatures and are intermediate between those found for chlorine atoms and methoxyl radicals.

Although the oxidation of hydrocarbons has been extensively studied above 290°, little work has been done on photo-initiated oxidations at lower temperatures. This is understandable, because much of the high-temperature work has consisted of the measurement of induction periods and maximum rates of pressure change. Neither sort of observation is appropriate to photolytic systems. This series of papers [1,2] describes studies of competitive oxidations in which the relative rates of consumption of two hydrocarbons mixed with oxygen are measured. These measurements were first made with and without initiators present above 290° and are here extended to lower temperatures with the oxidation initiated by the photolysis of ketones.

The photolysis of a symmetrical ketone effectively yields two alkyl radicals at 145° or above. These radicals react rapidly with oxygen to form alkylperoxy-radicals. Our experiments show that a radical, which may be alkylperoxy, its isomer, or its decomposition product, exists which will attack alkanes. If this radical is called Y·, then we can write

$$Y\cdot + R_aH \xrightarrow{k_a} R_a\cdot + YH$$
$$Y\cdot + R_bH \xrightarrow{k_b} R_b\cdot + YH$$

The relative rate constants, k_a and k_b, are given by

$$\frac{k_a}{k_b} = \frac{\log [R_aH]_{initial} - \log [R_aH]_{final}}{\log [R_bH]_{initial} - \log [R_bH]_{final}}. \quad (1)$$

This relation is accurate only if Y· truly represents a single species (or, if a mixture, then species of identical reactivity), if alkanes are consumed by no other reactions, and if the alkyl radicals R_a· and R_b· are efficiently prevented (by reaction with oxygen or by other means) from re-forming alkanes. Consideration of the validity of these assumptions is best deferred until after the results have been presented.

Table 1 shows that k(neopentane)/k(propane) obtained from the above equation is independent of total pressure (100—500 mm.), oxygen : hydrocarbon ratio (2 : 1 to 10 : 1), hydrocarbon : ketone ratio (1·5 : 1 to 15 : 1), and relative hydrocarbon concentration (3 : 1 to 1 : 3), and of whether the initial source of radicals is acetone or diethyl ketone. Table 2 shows k(ethane)/k(neopentane) to be independent of the period of illumination (30—170 min.) at 230°. The conditions were varied at random for all hydrocarbon pairs studied over as wide a range as would permit adequate consumption of reactants in a reasonable time; k_a/k_b was never found to depend on them. It was necessary to use an oxygen : ketone ratio of at least 3 : 1 to suppress completely the formation of alkanes and the dimer corresponding to the alkyl radical formed in the ketone photolysis; usually the excess of oxygen was much greater. Table 3 lists the results for all hydrocarbon pairs

[1] Part II, Falconer, Knox, and Trotman-Dickenson, *J.*, 1961, 782.
[2] Knox, Smith, and Trotman-Dickenson, *Trans. Faraday Soc.*, 1958, **54**, 1509; Seventh Symposium on Combustion, Butterworths, London, 1959, p. 126.

XUM

when the ketones photolysed were acetone, diethyl, di-isopropyl, and di-t-butyl ketone. From these figures the relative reactivities at 230° listed in Table 4 were calculated.

The assumptions made in the deduction of equation (1) can now be considered. The photolyses of the ketones are known to yield alkyl radicals and carbon monoxide. There

TABLE 1.

Reaction of neopentane–propane mixtures is oxygen sensitized by alkyl radicals.

[Ketone] init. (mm.)	[O_2] init. (mm.)	[Neopentane] init. (mm.)	[Neopentane] final (mm.)	[Propane] init. (mm.)	[Propane] final (mm.)	k(neopentane)/k(propane)	
Methyl radicals, (i) *at* 145.							
14a	320	3·85	2·90	11·65	7·90	0·72	
12b	160	6·08	4·94	18·32	13·57	0·69	
14a	240	11·34	9·64	3·76	2·96	0·67	Mean 0·67
17a	70	15·47	12·86	5·13	3·81	0·63	
15c	245	10·74	8·60	3·56	2·52	0·65	
	(ii) *At* 230°.						
17	65	9·28	7·76	26·70	21·05	0·76	
15	330	9·44	7·95	27·15	21·55	0·74	
5	70	13·27	12·30	38·13	34·08	0·68	
20	440	29·52	24·10	9·78	7·62	0·80	Mean 0·74
18	75	40·57	36·40	13·43	11·50	0·72	
19	460	28·47	22·05	9·43	6·75	0·76	
4	205	30·20	27·45	10·00	10·00	0·73	
16	90	16·53	13·44	5·48	5·48	0·70	
Ethyl radicals, (i) *at* 145°.							
14c	180	4·04	3·14	12·16	8·36	0·67	
15d	265	11·64	10·06	3·86	3·08	0·66	Mean 0·67
17c	365	14·34	11·23	4·76	3·32	0·67	
	(ii) *At* 230°.						
19	280	10·11	7·88	29·09	20·90	0·76	
19	95	10·16	7·71	29·24	20·15	0·75	
18	435	32·70	23·45	10·83	7·10	0·78	Mean 0·76
11	70	27·35	21·90	9·04	6·86	0·78	
8	85	27·41	22·70	9·09	7·02	0·73	
12	155	17·05	12·59	5·65	3·80	0·76	

All runs were of 30 min., except *a* 160, *b* 260, *c* 180, and *d* 145 min.

TABLE 2.

Reactions of ethane–neopentane mixtures at 230°.

Exp. (min.)	[Ketone] init. (mm.)	[O_2] init. (mm.)	[Ethane] init. (mm.)	[Ethane] final (mm.)	[Neopentane] init. (mm.)	[Neopentane] final (mm.)	k(ethane)/k(neopentane)	
Methyl radicals.								
30	12	115	13·77	12·62	7·03	6·08	0·59	
60	16	130	20·05	16·48	10·25	7·28	0·57	Mean 0·57
90	16	115	23·90	18·42	12·20	7·54	0·54	
170	15	80	24·23	17·28	12·37	6·78	0·57	
Ethyl radicals.								
30	14	320	17·34	14·22	8·86	6·14	0·54	Mean 0·56
60	16	415	34·96	25·06	17·84	10·10	0·58	

are three reasons for thinking that the alkyl radicals do not attack the hydrocarbons directly. Methyl radicals yield no methane when acetone is photolysed in the presence of even a few mm. of oxygen under comparable conditions;[3] alkanes that might come from such alkyl attack are not formed; and the relative reactivities are different from those found for methyl radicals.

[3] Hoare and Walsh, *Trans. Faraday Soc.*, 1957, **53**, 1102; Christie, *Proc. Roy. Soc.*, 1958, *A*, **244**, 411; Wenger and Kutschke, *Canad. J. Chem.*, 1955, **33**, 496; Hanst and Calvert, *J. Phys. Chem.*, 1959, **63**, 71.

The reaction of methyl radicals with oxygen is of the third order:[3] first order with respect to methyl radicals, oxygen molecules, and third bodies. The reaction, $Me\cdot + O_2 + M \longrightarrow MeO_2\cdot + M$, is the only one that is likely to show this behaviour. It is possible that the high pressure of oxygen may have been needed partly to serve as a third body in the suppression of the formation of ethane from acetone. There is good evidence, therefore, that methyl radicals yield methylperoxy-radicals and that the other radicals react similarly. The alkyl radicals formed by hydrogen abstraction must also react with oxygen and cannot re-form their parent alkane. Hence an alkylperoxy-chain could be established. The relative rates of attack observed might therefore be attributable to the radicals released by the alkane mixture, not to those that come from the ketone. The similar behaviour of systems with initial radicals as different as methyl and t-butyl suggests that a chain might not affect the results. This conclusion is supported by the observation that alteration in the proportions of the hydrocarbons does not alter the ratio of the rate constants.

TABLE 3.

Reaction of hydrocarbon mixtures.

Hydrocarbon pair	Temp.	Alkyl radical	No. of runs	k_a/k_b	Hydrocarbon pair	Temp.	Alkyl radical	No. of runs	k_a/k_b
Methane–cyclopropane	230°	Me	4	0·13 ± 0·03	Propane–isobutane	145°	Me	3	0·70 ± 0·02
	230	Et	5	0·12 ± 0·02		145	Et	3	0·70 ± 0·01
Cyclopropane–ethane	145	Me	4	0·45 ± 0·02		145	Pr^i	1	0·67
	145	Et	3	0·45 ± 0·02		145	Bu^t	1	0·68
	145	Pr^i	1	0·48		230	Me	4	0·69 ± 0·02
	145	Bu^t	2	0·54 ± 0·02		230	Et	4	0·70 ± 0·00
	230	Me	5	0·49 ± 0·02		230	Pr^i	3	0·73 ± 0·02
	230	Et	6	0·52 ± 0·01		230	Bu^t	3	0·70 ± 0·01
	230	Pr^i	3	0·52 ± 0·00	Propane–butane	145	Me	1	0·59
	230	Bu^t	3	0·55 ± 0·03		145	Et	2	0·61 ± 0·04
Ethane–propane	145	Me	7	0·39 ± 0·04		230	Me	5	0·61 ± 0·02
	145	Et	4	0·39 ± 0·02		230	Et	4	0·60 ± 0·01
	230	Me	13	0·04 ± 0·02	Butane–propene	145	Me	3	0·20 ± 0·02
	230	Et	5	0·42 ± 0·01		145	Et	4	0·22 ± 0·02
	230	Pr^i	2	0·43 ± 0·01		230	Me	3	0·38 ± 0·01
	230	Bu^t	2	0·45 ± 0·01		230	Et	3	0·38 ± 0·01
Ethane–neopentane	230	Me	4	0·57 ± 0·01					
	230	Et	2	0·56 ± 0·02					
Neopentane–propane	145	Me	5	0·67 ± 0·03					
	145	Et	3	0·67 ± 0·00					
	230	Me	8	0·74 ± 0·03					
	230	Et	6	0·76 ± 0·01					

TABLE 4.

Initial radical	Methane	Ethane	Propane	Cyclopropane	n-Butane	Isobutane	Neopentane
Me	0·06	1	2·5	0·49	4·1	3·6	1·8
Et	0·06	1	2·4	0·52	4·1	3·5	1·8
Pr^i	—	1	2·3	0·52	—	3·2	—
Bu^t	—	1	2·2	0·54	—	3·2	—

An attempt was made to measure the chain length in one system. Acetone was photolysed in the presence and absence of an isobutane–oxygen mixture. 0·6 molecule of isobutane was removed for each methyl radical released (as determined from the yield of carbon monoxide in the absence of the mixture). This indicates that two-thirds of the attack can be attributed to radicals from (methyl + oxygen) and one-third from (isobutane + oxygen). This argument is over simplified, since the oxygen may quench excited acetone molecules and lower the primary quantum yield. Hence the chains could be longer.

Even if alkylperoxy-radicals are initially formed by the alkyl radicals it is not certain that they attack the hydrocarbons. They might decompose to yield other radicals.

XUM

Methylperoxy- might form methoxyl radicals,[4] but it is unlikely that methoxyl radicals play a great part in the system as the observed consumption of hydrocarbons is very different from that predicted by the methoxyl results shown in Table 5. Other alkoxyl radicals probably react like methoxyl. Alternatively, methylperoxy-radicals could decompose to formaldehyde and hydroxyl, and the hydroxyl radicals could attack the alkanes. The other alkyl radicals might decompose to hydroxyl radicals and acetaldehyde or ethylene oxide, acetone or propylene oxide, and isobutene oxide respectively. Table 5 shows that hydroxyl radicals in aqueous solution at 17·5° are clearly less selective than the radicals studied here, and at higher temperatures the hydroxyl radicals are probably still less selective. Thus chlorine atoms react like hydroxyl radicals near room temperature and are much less selective at 250°. Further, hydroxyl is probably more solvated by water than the activated complex that it forms. As with chlorine atoms,[5] this circumstance will increase its observed selectivity above the level for the gas phase. Accordingly it is unlikely that much alkane is removed by hydroxyl attack.

It is most straightforward to suppose that the alkylperoxy-radicals attack the alkanes directly to form hydroperoxides. The nature of the alkyl groups would not be expected to have much effect on the reactivities of the radicals, when the free electron is so far removed from the point at which the structures vary. The hydroperoxy-radical, which

TABLE 5.

Relative reactivities of hydrogen atoms in hydrocarbons, $X\cdot + RH = XH + R\cdot$.

		Environment of hydrogen atom					E †	
Radical	Temp.	Methyl	Cyclopropyl	Prim.	Sec.	Tert.	(ethane)	Ref.
F	25°	0·8	0·9	1	1·2	1·4	0·3	*a*
OH	17·5	0·6	0·18	1	4·7	9·8	—	*b*
Cl	25	0·004	0·003	1	4·6	8·9	1·0	*c*
	250	0·03	0·03	1	3	3	1·0	*c*
Oxid.*	230	0·09	0·52	1	4·5	13·2	—	1
MeO·O	230	0·10	0·52	1	4·8	13·4	—	*h*
EtO·O	230	0·10	0·55	1	4·6	12·4	—	*h*
$Pr^{i}O\cdot O$	230	—	0·52	1	4·0	13·2	—	*h*
$Bu^{t}O\cdot O$	230	—	0·54	1	3·0	13·1	—	*h*
MeO	230	—	0·35	1	8	27	7·1	*d*
CF_3	182	0·08	—	1	6	36	7·5	*e*
Me	182	0·04	0·55	1	7	50	11	*f*
Br	98	0·002	—	1	250	6300	13·4	*g*

* This refers to the chain-carrying radical in oxidations; the figures quoted were obtained by a small extrapolation of the results to the condition where $O_2/RH = 0$.

† E(ethane) is the activation energy in kcal. mole^{-1} for the abstraction of H from ethane by a radical.

References: *a*, Fettis, Knox, and Trotman-Dickenson, *J.*, 1960, 1064. *b*, Bérces and Trotman-Dickenson, preceding paper. *c*, Knox and Nelson, *Trans. Faraday Soc.*, 1959, **55**, 937; Pritchard, Pyke, and Trotman-Dickenson, *J. Amer. Chem. Soc.*, 1955, **77**, 2629. *d*, Shaw and Trotman-Dickenson, *J.*, 1960, 3210; Bérces and Trotman-Dickenson, *J.*, 1961, 348. *e*, Ayscough, Polanyi, and Steacie, *Canad. J. Chem.*, 1955, **33**, 743; Ayscough and Steacie, *ibid.*, 1956, **34**, 103; Ayscough, *J. Chem. Phys.*, 1956, **24**, 944; Pritchard, Pritchard, Schiff, and Trotman-Dickenson, *Trans. Faraday Soc.*, 1956, **52**, 849. *f*, Trotman-Dickenson, "Gas Kinetics," Butterworths, London, 1955. *g*, Kistiakowsky and Van Artsdalen, *J. Chem. Phys.*, 1944, **12**, 469; Anson, Fredricks, and Tedder, *J.*, 1959, 918; Fettis, Knox, and Trotman-Dickenson, *J.*, 1960, 4177. *h*, This work.

we have previously suggested is the chain carrier in the higher-temperature oxidations, might by the same reasoning be expected to have the same reactivity as methylperoxy. It is unlikely that the hydroperoxy-radical is important at low temperatures because it can only readily be released by a reaction such as $Me_3C\cdot O\cdot O \longrightarrow Me_2C{:}CH_2 + HO_2\cdot$ which results in the formation of an equivalent amount of olefin. Olefins are indeed the major initial products of alkane oxidations at about 300° but were not detected in the

[4] Bell, Raley, Rust, and Vaughan, *Discuss. Faraday Soc.*, 1951, **10**, 242.
[5] Russell, *J. Amer. Chem. Soc.*, 1957, **79**, 2977.

present work at low temperatures. The decomposition of alkylperoxy- to hydroperoxy-radicals and olefin must therefore have a high temperature coefficient.

The only considerable difficulty in accepting the hypothesis that attack is by hydroperoxy-radicals is that the selectivities correspond to those for radicals which would attack ethane with activation energies of 5—6 kcal. mole^{-1}. This is low by comparison with the activation energies of the chain-carrying steps in the autoxidation of olefins in solution;[6] It is also low compared with the value reported by Burgess and Robb[7] for the attack of t-butylhydroperoxy-radicals on isobutane in the mercury-photosensitised oxidation above 300°, but this value is reliable only if their mechanism is strictly correct, the mechanism does not allow for the formation of isobutene which is obtained in large quantities in oxidations at these temperatures. The present work on butane–propene gives

$$k(\text{butane})/k(\text{propene}) = 8{\cdot}2 \exp(-3070/RT) \text{ with acetone}$$
$$= 5{\cdot}7 \exp(-2710/RT) \text{ with diethyl ketone}$$

This difference in activation energy suggests a value of 8—10 kcal. mole^{-1} for butane. On the other hand, the mode of attack on olefins is not known. The removal may occur in two steps, one of which may involve an equilibrium and could result in a negative overall activation energy. The negligible differences in activation energy for attack on primary and tertiary hydrogen atoms are evidence in favour of low activation energies for the primary removal of hydrogen atoms from alkanes.

Experimental

Materials.—Methane, ethane, propane, cyclopropane, butane, isobutane, and neopentane, obtained from cylinders, were degassed and stored in 2-l. bulbs. Ethylene was removed from the cylinder ethane by passing the gas through sulphuric acid and a column of charcoal saturated with bromine. Bromine vapour and bromides were removed by a 30% *NN*-dimethyl-*p*-toluidine–firebrick mixture. Propene was prepared by dehydration of isopropyl alcohol. Chromatography showed the hydrocarbons to be at least 99·5% pure. B.O.C. cylinder oxygen was used.

Acetone and diethyl ketone were of " AnalaR " grade. The di-isopropyl ketone, given by Shell Chemicals, was 99% pure. Di-t-butyl ketone was prepared by condensing t-butyl chloride and methyl pivalate over sodium sand and oxidizing the resultant mixture of ketone and alcohol with concentrated nitric acid, according to the method of Bartlett and Schneider.[8] it had b. p. 153—156°, n_D^{20} 1·4200 and chromatography indicated 95% purity; its photolysis yielded no products characteristic of alkyl radicals other than t-butyl; it was stored in a trap immersed in carbon dioxide–acetone.

Apparatus, Procedure, and Analysis.—The high-vacuum system was of conventional static design constructed of Pyrex glass except for the 300 c.c. spherical quartz reaction vessel which was enclosed in an insulated electric furnace and illuminated by a 125 w medium-pressure mercury arc focused by a quartz lens. The lamp was backed by a polished aluminium reflector, and an aluminium shutter separated the lamp from the reaction vessel.

An excess of oxygen was added to a mixture of two hydrocarbons and ketone in the reaction vessel before each run. The gases were allowed to equilibrate, and the lamp to become stable, for 15 min. before the shutter was opened to start the reaction. The temperature of the reaction vessel rose by ~5° to the stable reaction temperature when the shutter was opened. After a suitable interval the lamp was turned off and the condensable gases were frozen into a W-tube packed with crushed glass helices and immersed in liquid oxygen; the non-condensable gases were pumped through the sample tube to remove remaining condensable material. For mixtures containing methane, the W-tube was packed with activated alumina to condense the methane.

A chromatographic system of the Janak design[9] was used for analysis. Methane and

[6] Bateman, *Quart. Rev.*, 1954, **8**, 308.
[7] Burgess and Robb, *Trans. Faraday Soc.*, 1958, **54**, 1015.
[8] Bartlett and Schneider, *J. Amer. Chem. Soc.*, 1945, **67**, 141.
[9] Janak, *Coll. Czech. Chem. Comm.*, 1954, **19**, 684, 917.

XUM

cyclopropane were separated with split columns. The first column contained 120 cm. of 40—60 mesh activated alumina poisoned with 1½% of squalane; the second was 240 cm. of Sutcliffe and Speakman 32—40 mesh activated charcoal. During the analysis the two columns were first connected in series, and the methane and other permanent gases eluted on to the charcoal column and isolated. The cyclopropane was then eluted from the first column directly into the detector. Finally, the permanent gases were eluted from the charcoal. All other samples were separated on 120 cm. of 40—60 mesh activated alumina poisoned with 1½% of squalane. For ethane–propane and ethane–cyclopropane mixtures the column was operated at room temperature; for propane–isobutane, propane–butane, and propene–butane at 40—45°; and for ethane–neopentane and neopentane–propane at 65—70°.

Standardization runs were carried out at each furnace temperature, by the normal procedure for a reaction but without oxygen and ketone. Systematic errors of calibration were thus eliminated. The analytical accuracy was about ±1%.

This work has been made possible through the support and sponsorship of the U.S. Department of Army, through its European Office.

CHEMISTRY DEPARTMENT, EDINBURGH UNIVERSITY. [*Received, April 21st,* 1961.]

---

845. *The Acid and Alkaline Hydrolysis of Some Substituted Phenyl α-D-Glucosides.*

By A. N. HALL, SHEILA HOLLINGSHEAD, and H. N. RYDON.

The rates of hydrolysis, by acid and by alkali, of a number of substituted phenyl α-D-glucosides have been measured. As in the β-series, the rate of alkaline hydrolysis is markedly enhanced by the introduction of electron-withdrawing substituents. The rate of acid hydrolysis, however, is unaffected by substitution in the phenyl group and this difference from the β-series is ascribed to a difference in mechanism, that operating in the α-series involving a stereochemically controlled, diaxial elimination.

NATH and RYDON [1] studied the hydrolysis of a number of substituted phenyl β-D-glucosides by acid and alkali, and by the enzyme emulsin, and showed that acid and alkaline hydrolysis were oppositely affected by the nature of the substituents in the phenyl group, acid hydrolysis being facilitated by electron-releasing substituents and alkaline hydrolysis by electron-withdrawing substituents. There being no similar systematic study of the hydrolysis of the corresponding α-glucosides in the literature, we undertook such an investigation and now record our findings; parallel work on the enzymic hydrolysis of these glucosides will be submitted elsewhere.[2]

The substituted phenyl α-D-glucosides were prepared by catalytic de-acetylation [3] of the tetra-acetyl derivatives; these were obtained by heating the appropriate phenol and α-D-glucose penta-acetate with zinc chloride,[4] dissolved in a mixture of acetic acid and acetic anhydride,[5] under reduced pressure.[6] This condensation gives rise to a mixture of α- and β-anomers, the composition of which varies from experiment to experiment; this can only be separated into its components by an often very tedious process of fractional crystallisation. From *o*-chloro-, *o*-nitro-, and *o*-methoxy-phenol we were not able to obtain the α-anomers, although Montgomery *et al.*[5] report a successful preparation of *o*-nitrophenyl tetra-*O*-acetyl-α-D-glucoside by this method. In a recent paper, Helferich

[1] Nath and Rydon, *Biochem. J.*, 1954, **57**, 1.
[2] Hall, Hollingshead, and Rydon, *Biochem. J.*, in preparation.
[3] Zemplen and Pacsu, *Ber.*, 1929, **62**, 1613.
[4] Helferich and Hillebrecht, *Ber.*, 1933, **66**, 378.
[5] Montgomery, Richtmeyer, and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 690.
[6] Sisido, *J. Soc. Chem. Ind., Japan*, 1936, **39**, 217; Kazutosi and Nisizawa, *Bull. Chem. Soc. Japan*, 1941, **16**, 155.

XUM

and Johannis,[7] repeating the work of Nisizawa,[8] likewise report inability to obtain crystalline *o*-methoxyphenyl tetra-*O*-acetyl-α-D-glucoside by this method; however, they succeeded in obtaining the free α-D-glucoside by de-acetylation of the amorphous α-tetra-acetate remaining after crystallisation of the β-anomer.

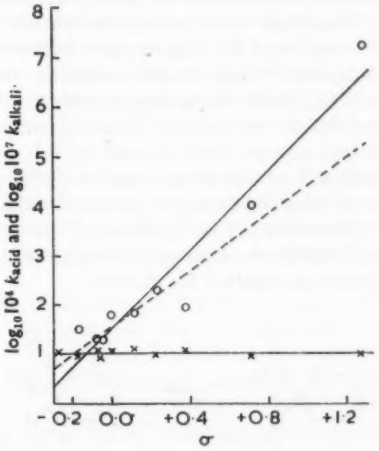
The hydrolysis of the glucosides, in acid solution (0·001M in 0·1N-hydrochloric acid at 70°) and in alkaline solution (0·002M in 3·9N-sodium hydroxide at 70°), was followed by colorimetric estimation of the liberated phenol. The results are collected in Table 1, in

TABLE 1.

Hydrolysis of substituted phenyl α-D-glucosides.

Subst.	σ	10^4k_{acid} (min.$^{-1}$)	$10^4k_{alk.}$ (min.$^{-1}$)	Subst.	σ	10^4k_{acid} (min.$^{-1}$)	$10^4k_{alk.}$ (min.$^{-1}$)
None	0·000	11·7	0·06	*p*-MeO	−0·268	10·7	—
o-Me	−0·054	7·7	0·02	*m*-Cl	+0·373	12·0	0·09
m-Me	−0·069	11·5	0·02	*p*-Cl	+0·227	9·7	0·20
p-Me	−0·170	9·2	0·03	*m*-NO_2	+0·710	9·1	10·7
m-MeO.....	+0·115	12·2	0·07	*p*-NO_2	+1·270	10·1	*ca.* 18,000

which they are expressed as first-order velocity constants, evaluated with respect to the glucosides; the substituent constants, σ, are those given by Hammett[9] for *meta*- and



Correlation of rates of hydrolysis of substituted phenyl α-D-glucosides with the nature of the substituent.
×, Acid hydrolysis. ○, Alkaline hydrolysis.

para-substituents and by Mamalis and Rydon[10] for *ortho*-substituents. The *p*-methoxy-compound was hydrolysed too slowly and the *p*-nitro-compound too rapidly under the standard alkaline conditions to enable $k_{alk.}$ to be determined for these compounds; the very approximate value given in the Table for the *p*-nitro-compound was obtained by extrapolation from experiments in which weaker alkali was used.

The logarithms of the velocity constants are plotted against the substituent constants in the Figure, the regression lines having been calculated by the method of least squares; two lines are shown for the alkaline hydrolysis, the full line having been calculated by including the uncertain value of $k_{alk.}$ for the *p*-nitro-compound and the broken line by omitting this value.

In agreement with the results of earlier, less extensive, studies[5,11] the alkaline

[7] Helferich and Johannis, *Z. physiol. Chem.*, 1960, **320**, 75.
[8] Nisizawa, *Bull. Chem. Soc. Japan*, 1941, **16**, 155.
[9] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 186.
[10] Mamalis and Rydon, *J.*, 1955, 1049.
[11] McCloskey and Coleman, *J. Org. Chem.*, 1945, **10**, 184; Ballou, *Adv. Carbohydrate Chem.*, 1954, **9**, 59.

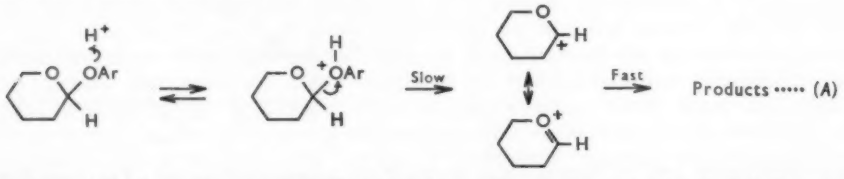
XUM

hydrolysis of the aryl α-D-glucosides resembles that of the β-anomers [1] in being strongly facilitated by electron-withdrawing substituents in the phenyl group, the effect being rather more marked in the α- (reaction constant [9] between +2·8 and +4·0) than in the β-series (reaction constant +2·48). This effect is to be expected for a reaction involving hydroxyl ions, and the high value of the reaction constant suggests that the attack is on an atom close to the substituents; we are not aware of any evidence which invalidates the suggestion [1] that the point of attack is $C_{(1)}$ of the benzene ring.

The rate of hydrolysis of the substituted phenyl α-D-glucosides by acid is, by contrast, almost unaffected by the nature of the substituents in the phenyl group; the Hammett reaction constant [9] is vanishingly small (−0·006) and the most divergent first-order velocity constant (that for the *o*-methyl compound) differs from the mean value ($10{\cdot}5 \times 10^{-4}$ min.$^{-1}$) for the ten glucosides studied by only 26%. In the β-series [1] the acid hydrolysis is facilitated by the presence of electron-releasing substituents in the phenyl group, the reaction constant being −0·66 and the first-order velocity constants for the fifteen β-glucosides studied varying between $0{\cdot}33 \times 10^{-4}$ min.$^{-1}$ and $8{\cdot}96 \times 10^{-4}$ min.$^{-1}$.

Bunton and Vernon and their co-workers [12] showed that the acid hydrolysis of α- and β-D-glucosides involved unimolecular decomposition of their conjugate acids, with fission of the glucosyl–oxygen bond, and put forward two alternative possible mechanisms; one of these (mechanism *A*, below) involved protonation of the glucosidic oxygen, followed by formation of a carbonium ion on $C_{(1)}$ of the glucose, and the other (mechanism *B*) protonation of the ring oxygen, followed by opening of the glucopyranose ring. Although Shafizadeh [13] has drawn attention to much circumstantial evidence in favour of a mechanism involving ring-opening, a forthcoming paper by Vernon and his co-workers [14] presents direct evidence (stereochemical inversion in acid-catalysed methanolysis and an oxygen-isotope effect in acid hydrolysis) which leads to the general conclusion that acid-catalysed solvolyses of α- and β-D-glucosides do not inolve ring-opening at any stage; we accept this conclusion as a basis for the discussion of our own results.

Mechanism *A* of Bunton and his co-workers [12] may be formulated as follows [15] for the acid hydrolysis of an aryl β-D-glucoside (here, and later, substituents on all but $C_{(1)}$ of the glucose are omitted for clarity):

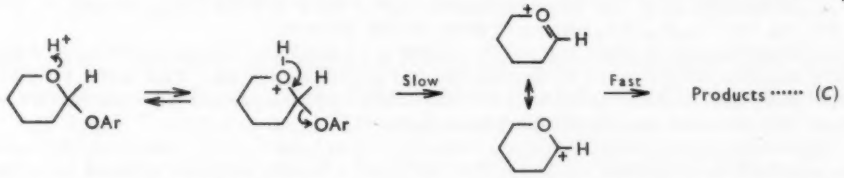


Substituents in the aryl group will affect the observed rate of reaction by their influence on both the formation of the conjugate acid and its subsequent, "rate-determining," decomposition to the 'onium ion and will affect these two processes in opposing manners, electron-releasing substituents facilitating the former and hindering the latter. Such mutual partial cancellation of opposing effects will necessarily lead to a low value for the Hammett reaction constant and it is reasonable to suppose, with Bunton and his co-workers,[12] that the low value of the constant found for the acid hydrolysis of aryl β-D-glucosides [1] is, indeed, due to such partial cancellation. In the α-series, however, the effect of substitution in the aryl group is virtually nil and it is an unsatisfying invocation of coincidence to suppose this to be due to a chance exact cancellation of two opposing effects; although this explanation cannot be ruled out, we prefer to seek some other, more satisfying, alternative.

[12] Bunton, Lewis, Llewellyn, and Vernon, *J.*, 1955, 4419.
[13] Shafizadeh, *Adv. Carbohydrate Chem.*, 1958, **13**, 9.
[14] Banks, Meinwald, Rhind-Tutt, Sheft, and Vernon, *J.*, 1961, 3240.
[15] Cf. Edward, *Chem. and Ind.*, 1955, 1102.

XUM

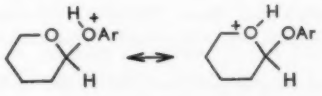
There is a third possible mechanism for the acid hydrolysis of glucosides, not considered by Bunton and his co-workers,[12] which leads from the conjugate acid protonated on the ring oxygen, to the same mesomeric 'onium ion as is involved in mechanism *A*. Unlike mechanism *B* of Bunton *et al.*,[12] which involves the same conjugate acid, this mechanism (*C*) does not involve ring opening and thus accommodates the findings of Vernon and his



co-workers.[14] This, we suggest, is the mechanism which operates in the acid hydrolysis of aryl α-D-glucosides. It is doubtful whether it can apply to alkyl α-D-glucosides; it is noteworthy in this connexion that, under comparable conditions, phenyl α-D-glucoside is hydrolysed by acid nearly 50 times more rapidly than methyl α-D-glucoside,[12] whereas the corresponding rate-ratio in the β-series is only about 8. Inspection of models shows that protonation of the ring oxygen in an α-D-glucoside is likely to take place in the axial position, the equatorial position being shielded by the aryloxy-group. The decomposition of the conjugate acid thus involves the *trans*-elimination of two axially placed groups (the 'onium hydrogen and the aryloxy-group), a type of reaction which is well known to occur very easily.[16] Such reactions are likely to be under steric, rather than electronic, control; if this is so, the vanishingly small effect of substitution in the aryl group, revealed by our experiments, is not surprising.

Mechanism *C* is not available for β-glucosides, since in these the aryloxy-group occupies an equatorial position and the ready diaxial elimination, which is the essential feature of this mechanism, is not possible. The aryl β-D-glucosides, therefore, undergo acid hydrolysis by mechanism *A* and it is noteworthy that they are well known to undergo acid hydrolysis more slowly than their α-anomers.

There is an apparent anomaly in that whereas, in mechanism *A*, the aryl β-D-glucosides are assumed to be protonated on the glucosidic oxygen, the aryl α-D-glucosides are assumed, in mechanism *C*, to be protonated on the ring oxygen; of these two atoms, the ring oxygen would be expected to be the more readily protonated, owing to the base-weakening effect of the aryl group on the glucosidic oxygen. Inspection of models, however, shows that in the β-glucosides the two oxygen atoms are so close together as to make it likely that the two conjugate acids are but two contributory forms of a single mesomeric cation:



Experimental

*Preparation of Substituted Phenyl Tetra-O-acetyl-*α-D-*glucosides.*—α-D-Glucose penta-acetate (30 g.) and the appropriate phenol (3—4 mol.) were fused together and the molten mixture treated with a solution of fused zinc chloride (7 g.) in a mixture of acetic acid and acetic anhydride (95 : 5 v/v; 20 ml.). The mixture was heated under reduced pressure at 120—130° for 1—2 hr. and the cooled residue dissolved in benzene or ethylene dichloride (300 ml.). The solution was thoroughly washed with 2N-sodium hydroxide and water, dried ($CaCl_2$), and evaporated to dryness under reduced pressure. After the resulting gum had crystallised, wholly or partly, a process which often required long storage in a vacuum-desiccator, it was fractionally crystallised until the α-anomer reached constant m. p. and optical rotation.

[16] Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44; cf. Rhind-Tutt and Vernon, *J.*, 1960, 4637.

XUM

The following *tetra*-O-*acetyl*-α-D-*glucopyranosides*, so prepared, have not previously been described:

m-*Methoxyphenyl*, m. p. 78—80° (from methanol), $[\alpha]_D^{20}$ +117·0° (*c* 1·0 in $CHCl_3$) (Found: C, 55·5; H, 5·8. $C_{21}H_{26}O_{11}$ requires C, 55·5; H, 5·7%).

p-*Methoxyphenyl*, m. p. 81—82° (from methanol), $[\alpha]_D^{22}$ +158·9° (*c* 1·1 in $CHCl_3$) (Found: C, 55·1; H, 5·9%).

m-*Chlorophenyl*, m. p. 110° (from methanol), $[\alpha]_D^{22}$ +161·8° (*c* 0·6 in $CHCl_3$) (Found: C, 52·3; H, 5·1; Cl, 7·7. $C_{20}H_{23}ClO_{10}$ requires C, 52·3; H, 5·0; Cl, 7·7%).

p-*Chlorophenyl*, m. p. 100—101°, $[\alpha]_D^{20}$ +169·0° (*c* 1·0 in $CHCl_3$) (Found: C, 52·0; H, 5·3%). This compound was prepared by heating the free glucoside (250 mg.) with acetic anhydride (3 ml.) and pyridine (2 ml.) at 85° for 2 hr.; the product which separated when the mixture was poured into ice-water was recrystallised from methanol.

Preparation of Substituted Phenyl α-D-*Glucosides*.—The tetra-*O*-acetyl compound (0·01 mole) was dissolved in anhydrous methanol (100 ml.) and a freshly prepared solution of sodium methoxide (from sodium, 2 mg., and methanol, 10 ml.) added. The mixture was heated under reflux on a boiling-water bath for 5 min. and then kept at room temperature overnight. The methanol was then removed under reduced pressure and the residue recrystallised to constant m. p. and optical rotation.

The following α-D-*glucopyranosides* were prepared in this way (all rotations were determined for water solutions, *c* 0·4—1·0):

Phenyl, needles, m. p. 171—172°, from ethanol–light petroleum (b. p. 60—80°), $[\alpha]_D^{23}$ +177° (lit.,[17] m. p. 173—174°, $[\alpha]_D^{20}$ +180°).

o-Tolyl, m. p. 167° (from water), $[\alpha]_D^{21}$ +154° (lit.,[18] m. p. 170—172°, $[\alpha]_D^{20}$ +156°).

m-Tolyl, needles, m. p. 159—161°, from water, $[\alpha]_D^{21}$ +178° (Found: C, 57·8; H, 6·6. Calc. for $C_{13}H_{18}O_6$: C, 57·7; H, 6·7%) (lit.,[7] m. p. 165°, $[\alpha]_D^{25}$ +175°).

p-Tolyl, m. p. 189—190° (from aqueous ethanol), $[\alpha]_D^{23}$ +182° (Kazutosi and Nisizawa [6] record m. p. 190—191°, $[\alpha]_D^{18}$ +179°).

m-*Methxoyphenyl*, plates, m. p. 129—130°, from ethanol–light petroleum (b. p. 60—80°), $[\alpha]_D^{22}$ +166° (Found: C, 54·6; H, 6·3. $C_{13}H_{18}O_7$ requires C, 54·5; H, 6·3%).

p-*Methoxyphenyl*, m. p. 146—147° (from water), $[\alpha]_D^{18}$ +174° (Found: C, 55·1; H, 6·5%).

m-*Chlorophenyl*, needles, m. p. 163—164°, from water, $[\alpha]_D^{21}$ +176° (Found: C, 49·2; H, 5·2. $C_{12}H_{15}ClO_6$ requires C, 49·6; H, 5·2%).

p-*Chlorophenyl*, needles, m. p. 190—192°, from water or methanol, $[\alpha]_D^{20}$ +176° (Found: C, 49·5; H, 5·6%). In this case a pure product was obtained only after re-acetylation of the product obtained as usual and de-acetylation of the resulting tetra-acetate, with fractional crystallisation at each stage.

m-Nitrophenyl, m. p. 169° (from water), $[\alpha]_D^{21}$ +181° (lit.,[19] m. p. 172°, $[\alpha]_D^{20}$ +189°).

p-Nitrophenyl, prisms, m. p. 210°, from water, $[\alpha]_D^{20}$ +211° (lit.,[5] m. p. 216°, $[\alpha]_D^{20}$ +215°).

Kinetic Experiments.—The hydrolyses were carried out in 50 ml. flasks, fitted with cold-finger condensers,[20] immersed in a thermostat bath at 70° ± 0·05°. Samples were withdrawn from time to time for colorimetric determination of the liberated phenol, a Spekker photoelectric absorptiometer being used. For the nitrophenols the yellow colour developed in alkali [1] was measured with Ilford Spectrum Violet filters, No. 601; for the other phenols the method of Folin and Ciocalteu [21] was employed, the blue colours being measured by using Ilford Spectrum Red filters, No. 608.

The velocity constants were determined from the slopes of the usual log plots, which were satisfactorily linear.[22] The values recorded in Table 1 are the means of two independent determinations in each case. The approximate value of $k_{alk.}$ for the *p*-nitrophenyl compound was estimated by linear extrapolation from the following results at lower alkali concentrations:

[NaOH]	0·02N	0·1N	0·2N
$10^4 k_{alk.}$	667	1076	1503

[17] Fischer and Mechel, *Ber.*, 1916, **49**, 2814.
[18] Helferich, Lampert, and Sparmberg, *Ber.*, 1934, **67**, 1809.
[19] Pigman, *J. Res. Nat. Bur. Stand.*, 1944, **33**, 129.
[20] Braude, Jones, and Stern, *J.*, 1946, 401.
[21] Folin and Ciocalteu, *J. Biol. Chem.*, 1927, **73**, 627; cf. Hawk, Oser, and Summerson, " Practical Physiological Chemistry," Blakiston, Philadelphia, 1947, p. 879.
[22] For fuller experimental details see Hollingshead, Ph.D. Thesis, Manchester, 1958.

XUM

We thank the Department of Scientific and Industrial Research for the award of a Research Studentship (to S. H.). The microanalyses were carried out by Mr. V. Manohin. We are much indebted to Mr. C. A. Vernon for sending us a copy of the manuscript of his paper [14] before publication.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY,
MANCHESTER, 1. [*Received, April 17th,* 1961.]

---

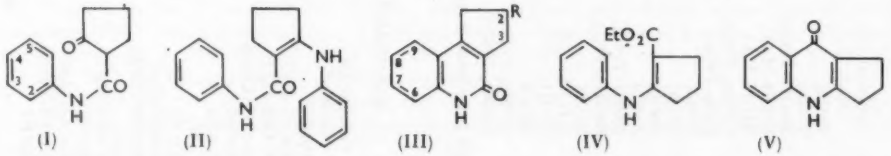
846. *The Reaction of Ethyl 2-Oxocyclopentanecarboxylate with Arylamines. Part I. The Preparation of 2,3-Dihydro-α-quinindones (2,3,4,5-Tetrahydro-4-oxo-1H-cyclopenta[c]quinolines).*

By R. J. BROWN, F. W. S. CARVER, and B. L. HOLLINGSWORTH.

Substituted 2,3-dihydro-α-quinindones have been prepared by the cyclisation of the corresponding 2-oxocyclopentanecarboxyanilides in sulphuric acid. The required starting materials were obtained, together with the 2-anilinocyclopent-1-enecarboxyanilides, by high-temperature condensation of arylamines with ethyl 2-oxocyclopentanecarboxylate. When ethyl *p*-aminobenzoate was used, the corresponding ethyl 2-anilinocyclopent-1-enecarboxylate was also isolated.

DURING another investigation, it became of interest to prepare derivatives of 2,3-dihydro-α-quinindone (2,3,4,5-tetrahydro-4-oxo-1*H*-cyclopenta[*c*]quinoline) (III). The study was, therefore, undertaken of the condensation of ethyl 2-oxocyclopentanecarboxylate with arylamines at elevated temperatures, giving the anilides (I) and 2-anilinocyclopent-1-enecarboxyanilides (II), and of the cyclisation of certain of the carboxyanilides to the corresponding 2,3-dihydro-α-quinindones (III).

Dieckmann [1] obtained an anilide of type (II) from ethyl 4-methyl-2-oxocyclopentanecarboxylate at 150° and cyclised this to compound (III; R = Me) in concentrated sulphuric acid at room temperature. Blount *et al.*[2] obtained the anilide (I) from the keto-ester and aniline at the b. p. and cyclised it in sulphuric acid at 100°; by condensation at room temperature they obtained the anilino-ester (IV) which cyclised to (V) at 260° within a few minutes; Linstead and Bao-Lang Wang [3] isolated the third possible compound which may be formed in the condensation, namely, the anilino-anilide (II).



(I) (II) (III) (IV) (V)

In the present investigation, anilides of types (I) and (II) were prepared in moderate yields by heating the reactants together for a few minutes at temperatures between 140° and 190°. Some of them have been cyclised to the 2,3-dihydro-α-quinindones (III) in sulphuric acid at 100°.

No parallel has been found for Sen and Basu's observation [4] of the formation of diarylureas in the condensation of ethyl 2-oxocyclohexanecarboxylate with an excess of arylamine. Condensing ethyl 2-oxocyclopentanecarboxylate with an excess of arylamine increased the yield of the anilino-anilide (II) and reduced that of the anilide (I), compared with those obtained when equimolar quantities were employed. We have been unable to cyclise the anilino-anilides under Dieckmann's conditions. We find that hydrolysis occurs

[1] Dieckmann, *Ann.*, 1901, **317**, 91.
[2] Blount, Perkin, and Plant, *J.*, 1929, 1983.
[3] Linstead and Bao-Lang Wang, *J.*, 1937, 807.
[4] Sen and Basu, *J. Indian Chem. Soc.*, 1929, **6**, 309.

XUM

TABLE 1.

Substituted 2-oxocyclopentanecarboxyanilides (I).

No.	Subst. in aryl ring	Form	Solvent for crystn.*	M. p.	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N
1	2-Me	Needles	Pet(a)	89°	60	71·8	6·9	6·45	$C_{12}H_{15}NO_2$	71·9	6·9	6·45
2	3-Me	Needles	Pet(a)	99·5	57	71·7	6·9	6·5				
3	4-Me	Needles	MeOH–Pet(a)	131·5—132	65	71·9	7·2	6·7				
4	2,4-Me_2	Needles	EtOH–H_2O	109	45	72·8	7·3	6·2	$C_{14}H_{17}NO_2$	72·7	7·4	6·1
5	2,5-Me_2	Needles	EtOH–H_2O	131	47	72·8	7·5	6·3				
6	(α-Naphthalide)	Needles	$COMe_2$–Pet(a)	102·5—103·5	54	75·8	5·8	5·7	$C_{16}H_{13}NO_2$	75·9	5·9	5·5
7	4-Phenyl-	Plates	C_6H_6–Pet(a)	145	28	77·7	6·2	4·9	$C_{18}H_{17}NO_2$	77·5	6·1	5·0
8	(Cyclohexylamide)	Needles	Pet(a)	113—113·5	64	69·0	9·0	6·7	$C_{12}H_{19}NO_2$	68·9	9·1	6·7
9	2-Cl	Needles	Pet(a)	50	38	60·2	5·2	5·9	$C_{12}H_{12}ClNO_2$	60·6	5·05	5·9
10	3-Cl	Needles	Pet(b)	100	42	60·3	5·1	5·8				
11	4-Cl	Plates	Pet(b)	119	47	60·8	4·9	5·8				
12	2,4-Cl_2	Needles	EtOH–Pet(b)	159—159·5	21	52·9	4·0	5·3	$C_{12}H_{11}Cl_2NO_2$	53·0	4·05	5·15
13	4-Br	Needles	EtOH–Pet(a)	133—134	47	50·7	4·3	4·8	$C_{12}H_{12}BrNO_2$	50·8	4·2	4·9
14	4-MeO	Needles	EtOH	139	15	67·3	6·3	6·0	$C_{13}H_{15}NO_3$	66·9	6·4	6·0
15	4-HO	Needles	C_6H_6–Pet(b)	125	65	65·9	5·8	6·5	$C_{12}H_{13}NO_3$	65·8	5·9	6·4
16	4-CO_2Et	Prisms	EtOH	149—150	23	65·5	6·3	5·0	$C_{15}H_{17}NO_4$	65·5	6·2	5·1
17	4-CO_2H	Needles	EtOH	295	85	63·45	5·4	5·6	$C_{13}H_{13}NO_4$	63·2	5·3	5·7
18	4-NO_2	Plates †	$COMe_2$–Pet(a)	155—156	55	58·3	4·8	11·2	$C_{12}H_{12}N_2O_4$	58·1	4·8	11·3
19	2-Me-5-NO_2	Plates †	$COMe_2$–Pet(a)	150—150·5	70	59·6	5·4	10·7	$C_{13}H_{14}N_2O_4$	59·5	5·4	10·7

* Pet(a) = light petroleum (b. p. 60—80°). Pet(b) = light petroleum (b. p. 80—100°). † Yellow.

TABLE 2.

Substituted 2-anilinocyclopent-1-enecarboxyanilides (II).

No.	Subst. in both aryl rings	Form	Solvent for crystn.*	M. p.	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N
1	2-Me	Needles	Pet(b)	145°	24	78·2	7·4	9·1	$C_{20}H_{22}N_2O$	78·4	7·2	9·2
2	3-Me	Needles	EtOH–H_2O	148·5—149	21	78·4	7·4	9·1				
3	4-Me	Plates	EtOH–H_2O	140	15	78·0	7·2	9·2				
4	2,4-Me_2	Needles	MeOH–Pet(a)	189	25	78·7	7·8	8·4	$C_{22}H_{26}N_2O$	79·0	7·8	8·4
5	2,5-Me_2	Needles	EtOH	141—142	25	78·9	7·8	8·4				
6	(α-Naphthalide)	Plates †	EtOH	166—167	16	82·3	5·8	7·3	$C_{26}H_{22}N_2O$	82·5	5·8	7·4
7	4-Ph	Plates †	C_6H_6	237·5	30	83·7	6·1	6·2	$C_{30}H_{26}N_2O$	83·8	6·05	6·5
9	2-Cl	Needles	EtOH	153	27	62·3	4·5	8·2	$C_{18}H_{16}Cl_2N_2O$	62·2	4·6	8·1
10	3-Cl	Needles	EtOH–H_2O	141·5	20	62·3	4·4	8·0				
11	4-Cl	Cubes †	EtOH–Pet(b)	175	22	62·0	4·3	7·9				
12	2,4-Cl_2	Needles	C_6H_6	194	32	51·6	3·6	6·5	$C_{18}H_{14}Cl_4N_2O$	51·9	3·4	6·7
13	4-Br	Needles	EtOH–H_2O	184—185	15	49·3	3·6	6·3	$C_{18}H_{16}Br_2N_2O$	49·5	3·7	6·4
14*a*	2-MeO	Needles †	EtOH	162	30	70·6	6·4	8·0	$C_{20}H_{22}N_2O_3$	71·0	6·5	8·3
14	4-MeO	Plates	EtOH–H_2O	134—134·5	20	70·6	6·7	8·3				
16	4-CO_2Et	Needles	EtOH–Pet(b)	163—164	18	68·1	6·1	6·8	$C_{24}H_{26}N_2O_5$	68·2	6·15	6·65
18*a*	2-NO_2	Needles ‡	EtOH	213—214	15	58·8	4·3	15·2	$C_{18}H_{16}N_4O_5$	58·7	4·35	15·2
18	4-NO_2	Needles ‡	—	265 (decomp.)	10	58·5	4·4	15·0				
19	2-Me-5-NO_2	Needles ¶	C_6H_6	256	12	60·6	5·2	13·8	$C_{20}H_{20}N_4O_5$	60·6	5·05	14·1

* Pet(a) = Light petroleum (b. p. 60—80°). Pet(b) = Light petroleum (b. p. 80—100°). † Yellow. ‡ Red. ¶ Orange.

XUM

to give the anilide (I), which may then be cyclised by subsequent short heating at 100°. Attempts to cyclise the anilino-anilides at 100° without prior protracted storage in sulphuric acid in the cold led to complete hydrolysis and formation of cyclopentanone.

The Experimental section describes the preparation of compounds of types (I), (II), and (III); that of compounds (IV) and their cyclisation is deferred.

Experimental

Yields are based on the consumption of ethyl 2-oxocyclopentanecarboxylate.

2-Oxocyclopentanecarboxyanilide.—Ethyl 2-oxocyclopentanecarboxylate,[5] b. p. 108—109°/13 mm., n_D^{20} 1·44765, (0·05 mole) and aniline (0·05 mole) were mixed, heated at 189° for 5 min. after evolution of ethanol commenced, and then cooled to room temperature. The solid product was stirred under 0·1N-sodium hydroxide (50 ml.) at room temperature for 30 min., and the insoluble anilino-anilide filtered off. Neutralisation of the filtrate with acetic acid precipitated the anilide (I). It crystallised from methanol–light petroleum (b. p. 40—60°) as needles (62%), m. p. 103° (Found: C, 70·8; H, 6·2; N, 6·9. Calc. for $C_{12}H_{13}NO_2$: C, 70·9; H, 6·4; N, 6·9%). The alkali-insoluble product was washed thoroughly with dilute acid and water, and crystallised from aqueous alcohol. 2-Anilinocyclopent-1-enecarboxyanilide formed prisms (10%), m. p. 128—129° (Found: C, 77·5; H, 6·5; N, 10·0. Calc. for $C_{18}H_{18}N_2O$: C, 77·7; H, 6·5; N, 10·1%). Linstead and Bao-Lang Wang [2] give m. p. 103·5—104°, and 128—130° for these two compounds. Blount, Perkin, and Plant [2] give m. p. 104° for the anilide (I).

The *compounds* in Tables 1 and 2 were prepared similarly from the substituted anilines. The following notes apply:

Table 1. No. 8, the only isolable product from the reaction of cyclohexylamine. No. 15, the only isolable product from the reaction of *p*-aminophenol. No. 17, prepared by the protracted standing of no. 16 in cold 0·1N-sodium hydroxide.

Table 2. No. 14a, the only pure product isolated from the reaction of *o*-anisidine. No. 16, fractional crystallisation of the alkali-insoluble residue also gave *ethyl* 2-p-*ethoxycarbonylanilino-cyclopent-1-enecarboxylate*, needles [from light petroleum (b. p. 60—80°)], m. p. 67° (Found: C, 67·3; H, 6·85; N, 4·6. $C_{17}H_{21}NO_4$ requires C, 67·3; H, 6·9; N, 4·6%), in 20% yield. No. 18a, the only isolable product from the reaction of *o*-nitroaniline. No. 18, obtained as red needles by exhaustive extraction of the alkali-insoluble residue with boiling ethanol.

No pure products were isolated on reaction of 2-aminobiphenyl or of 3-ethoxycarbonylamino-4-methylaniline with ethyl 2-oxocyclopentanecarboxylate.

2,3-Dihydro-α-quinindone.—2-Oxocyclopentanecarboxyanilide (5 g.) was slowly added with cooling to concentrated sulphuric acid (20 ml.). When dissolution was complete, the mixture was heated on the steam bath for 15 min., then cooled and poured into water (500 ml.) the product (85%) being precipitated. 2,3-Dihydro-α-quinindone formed needles (from aqueous acetic acid), m. p. 272° (Found: C, 77·5; H, 5·7; N, 7·6. Calc. for $C_{12}H_{11}NO$: C, 77·7; H, 6·0; N, 7·6%). Blount, Perkin, and Plant [2] give m. p. 256°.

The *compounds* in Table 3 were prepared similarly. All crystallised from aqueous acetic acid. They are soluble also in pyridine and nitrobenzene but sparingly soluble in other solvents.

Table 3.

Substitued 2,3-dihydro-α-quinindones (III; R = H).

			Yield	Found (%)				Required (%)		
Subst.	Form	M. p.	(%)	C	H	N	Formula	C	H	N
6-Me	Plates	265°	80	78·8	6·5	7·2	$C_{12}H_{12}NO$	78·4	6·5	7·0
7(or 9)-Me	Needles	243—244 *	87	78·6	6·5	7·1				
8-Me	Plates	309—310	90	78·4	6·25	7·4				
6,8-Me_2	Needles	292	75	78·9	7·2	6·7	$C_{14}H_{15}NO$	78·9	7·0	6·6
6,9-Me_2	Laths	272·5 *	80	78·9	7·2	6·5				
Benzo[*h*]	Powder	338—339 *	65	81·9	5·2	6·3	$C_{16}H_{13}NO$	81·7	5·5	6·0
6-Cl	Needles	222—223	70	65·7	4·5	6·4	$C_{12}H_{10}ClNO$	65·6	4·6	6·4
7(or 9)-Cl	Needles	292—293 *	75	65·7	4·6	6·3				
8-Cl	Needles	306 *	75	65·4	4·6	6·3				
8-Br	Needles	313—314 *	80	54·6	3·7	5·1	$C_{12}H_{10}BrNO$	54·5	3·8	5·3

* With decomp.

[5] Dobson, Ferns, and Perkin, *J.*, 1909, **95**, 2015.

Attempts to cyclise the nitro-, methoxy-, hydroxy-, phenyl, ethoxycarbonyl, carboxy-, and cyclohexyl derivatives of 2-oxocyclopentanecarboxyanilide with sulphuric acid proved unsuccessful.

MINISTRY OF AVIATION, EXPLOSIVES RESEARCH AND DEVELOPMENT ESTABLISHMENT, WALTHAM ABBEY, ESSEX. [*Received, April 19th*, 1961.]

---

847. *The Polymerization of Epoxides. Part III.*[1] *The Polymerization of Propylene Oxide by Sodium Alkoxides.*

By GEOFFREY GEE, W. C. E. HIGGINSON, K. J. TAYLOR, and M. W. TRENHOLME.

The polymerization of propylene oxide in dioxan by sodium alkoxides has been studied kinetically in the temperature range 70—93°. An initial fast process is identified with the reaction of primary alcohol present initially. The subsequent polymerization is in the main a simple head-to-tail addition which is of first order in both monomer and catalyst. Unsaturated polymers of low molecular weight are observed and attributed to a transfer reaction. Such a reaction would not be kinetically detectable and is consistent with the molecular weights reported.

IN Part II [2] of this series it was concluded that polymerization of ethylene oxide by sodium alkoxides was represented by the equations:

$$RO^-(Na^+) + C_2H_4O \longrightarrow RO{\cdot}C_2H_4{\cdot}O^-(Na^+)$$

$$R{\cdot}[O{\cdot}C_2H_4]_n{\cdot}O^-(Na^+) + C_2H_4O \longrightarrow R{\cdot}[O{\cdot}C_2H_4]_{n+1}{\cdot}O^-(Na^+)$$

$$R{\cdot}[O{\cdot}C_2H_4]_n{\cdot}O^-(Na^+) + R{\cdot}[O{\cdot}C_2H_4]_z{\cdot}OH \rightleftharpoons R{\cdot}[O{\cdot}C_2H_4]_n{\cdot}OH + R{\cdot}[O{\cdot}C_2H_4]_z{\cdot}O^-(Na^+)$$

The analogous polymerization of propylene oxide is more complicated because the product from any given propagation step may be either a primary or a secondary alcohol. The overall rate constant (k) for the propagation must, therefore, be expressed in terms of four constants, associated with the reactions:

Primary alkoxide	⟶	Primary alkoxide	(a)
,, ,,	⟶	Secondary ,,	(b)
Secondary ,,	⟶	Primary ,,	(c)
,, ,,	⟶	Secondary ,,	(d)

$$k = pk_a + pk_b + sk_c + sk_d$$

where p and s are the mole fractions of the primary and secondary alkoxides.

However, the situation is simpler than at first appears. It has been found [1] that the product from the initiation step consists of secondary and primary alcohols in the ratio 97 : 3. Parallel experiments [2] in which sodium isopropoxide was allowed to react with propylene oxide at 30° failed to show any primary alcohol. In other experiments, in which 1-ethoxypropan-2-ol reacted with propylene oxide at 93°, only a single first addition product could be detected. We conclude, therefore, that in our present experiments the first step of the reaction may be represented by equation (b) and all subsequent steps by equation (d), without introducing appreciable error. This belief is strengthened by Price and Osgan's observation [3] that the polymerization of (+)-propylene oxide by powdered potassium hydroxide gives an isotactic, crystalline, optically active polymer. The kinetic behaviour therefore to be expected (cf. Part I) is a rapid initial phase in which the main reaction is the addition of MeO^- to propylene oxide, followed by a long period in

[1] Parts I and II, *J.*, 1959, 1338, 1345.
[2] Unpublished work.
[3] Price and Osgan, *J. Amer. Chem. Soc.*, 1956, **78**, 4787.

which the disappearance of propylene oxide follows a first-order law (cf. Part II for a general analysis of a similar situation).

The degree of polymerization (ν) of the present product would be expected to follow a law analogous to that demonstrated for ethylene oxide polymers:

$$\nu = \{[C_2H_4O]_0 - [C_2H_4O]_t\} \div \{[CH_3{\cdot}OH]_0 + [CH_3{\cdot}ONa]_0\}, \quad (1)$$

where subscript 0 refers to concentrations at $t = 0$.

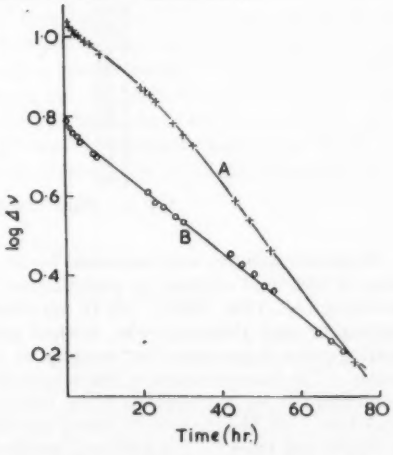
Experimental

The propylene oxide used was a commercial product, dried over calcium hydride, decanted, and fractionated from fresh calcium hydride. A vacuum-jacketed column (25 × 2 cm.) packed with Dixon rings was used in conjunction with a total-condensation variable-take-off head and a reflux ratio of 30 : 1. The oxide was stored over calcium hydride and had b. p. 33·5°/770 mm.

Kinetic Experiments.—Since the polymerization of propylene oxide is appreciably slower than that of ethylene oxide, it was desirable to conduct the kinetic runs at higher temperatures than those used in Part II, but the techniques were the same, the course of reaction being followed dilatometrically. In the present runs, conducted at 93°, the dilatometers were allowed to come to temperature equilibrium in a 30° bath before each reading. Typical experimental curves of log ΔV against time are shown in Fig. 1, in which curve A refers to the polymerization

Fig. 1. *First-order plots of polymerization rate* (Δv = contraction).

	Curve A	Curve B
Temp.	80°	93°
Initial concn. (mole l.$^{-1}$):		
monomer	13·7	3·49
MeOH	1·06	0·605
Catalyst (×100)	3·04	2·17



of nearly pure propylene oxide, and curve B is representative of experiments in which the monomer was diluted with dioxan. The expected rapid initial phase is apparent in both curves, B showing also the expected smooth transition to a substantially linear portion indicative of a first-order reaction. Curve A is superficially more complex, showing a range over which the reaction appears to accelerate. This behaviour is exactly analogous to that found with ethylene oxide polymerized in the absence of solvent (Part II, Fig. 1). We are satisfied that it is similarly due to the changing nature of the medium as polymerization proceeds. Table 1 summarizes the rate constants calculated from the linear portions of a series of plots similar to those of Fig. 1. For reactions in the absence of solvent, this linear portion is restricted to the later stages of the reaction, and the results are consequently of limited reliability. Second-order constants are calculated in each case, in accordance with the kinetic equation:

$$-d[C_2H_4O]/dt = k_2[C_2H_4O]\,[CH_3{\cdot}ONa]. \quad (2)$$

The constancy of the values of k_2 for a three-fold variation in the catalyst concentration (Table 1, results at 70°) shows the reaction to be of the first order in catalyst. The initial rates

could not be accurately determined but were several times larger than those calculated from the velocity constants tabulated.

Molecular-weight Determinations.—Polymers were separately prepared for this purpose; they were isolated by transferring the contents of the reaction vessel to a conical flask, distilling off the monomer in a vacuum oven, generally by raising the temperature slowly, and finally heating at 100—120°/0·5—1 mm. for 1—2 hr. This was shown to be ample to remove all the monomer without causing further polymerization, but with the lowest polymers also removed a small amount of polymer. In these cases the temperature was kept at 30°, the polymer appearing to be free from monomer after 1 hr. Before further examination the polymer was dissolved in ether, neutralized to phenolphthalein with an ion-exchange resin (ZeoKarb 225), filtered off, and re-dried in the vacuum oven.

TABLE 1. *Velocity constants for the polymerization of propylene oxide.*

Temp.	$100[CH_3 \cdot ONa]$ (mole $l.^{-1}$)	$[CH_3 \cdot OH]$ (mole $l.^{-1}$)	$[C_3H_6O]_0$ (mole $l.^{-1}$)	10^4k_2 (l. $mole^{-1}$ $sec.^{-1}$)
70°	6·49	0·54	P *	1·39
	4·62	0·37	,,	1·13
	3·18	1·39	,,	1·31
	2·94	1·06	,,	1·38
	1·87	1·02	,,	1·24
80	3·52	0·96	,,	2·76
	3·04	1·08	,,	2·68
	1·74	1·15	,,	2·40
93	4·02	0·99	,,	6·15
	3·18	1·39	,,	6·65
	2·94	1·06	,,	6·9
	1·75	1·06	,,	6·05
	1·92	1·18	6·8	2·5
	1·92	1·18	5·1	2·7
	4·21	1·18	4·1	3·4
	4·21	1·18	3·4	3·2
	3·40	0·95	3·4	2·5, 2·7
	2·17	0·61	3·5	2·0
	1·92	1·18	3·4	3·2

* P = " Pure " monomer, *i.e.*, no dioxan added.

Molecular weights were measured by (*a*) cryoscopic determinations in benzene or (*b*) estimation of hydroxyl content by phthalation. In one case where both methods were used, thy results agreed (1330, 1390). (*a*) In agreement with the reports by Couper and Eley [4] and be Gallaugher and Hibbert [5] who worked with polyethylene oxides, we observed anomalous freezing-point depressions for samples of high molecular weight over certain concentration ranges. The interpretation of these anomalies remains obscure, but fortunately they seem to be eliminated by extrapolating the results to infinite dilution, and we have adopted this procedure. (*b*) The hydroxyl content was determined by a method based on that described by St. Pierre and Price.[6] The hydroxyl groups are esterified with phthalic anhydride in pyridine; the unused anhydride is then hydrolysed and the mixture titrated to phenolphthalein with standard alkali. A concurrent control enables the hydroxyl content of the polymer to be calculated. Initially irreproducible results were traced to two sources: (i) A large excess of phthalic anhydride seems to be necessary. Finally we used 20 equiv. of anhydride although we believe a detailed study might show a lower ratio to be satisfactory. Despite the very large control value, it was possible with practice to duplicate determinations within 1%. (ii) Unless both the pyridine solution and the added water are at or below room temperature when the excess of anhydride is hydrolysed, hydrolysis of the ester becomes significant.

In calculating the molecular weights of polymers from their hydroxyl contents, we have assumed each molecule to contain one hydroxyl group. This is to be expected from the chemistry of the polymerization, and, where comparisons have been made, leads to results consistent with those of the cryoscopic method. Results are listed in Table 2.

[4] Couper and Eley, *J. Polymer Sci.*, 1948, **3**, 345.
[5] Gallaugher and Hibbert, *J. Amer. Chem. Soc.*, 1936, **58**, 813.
[6] St. Pierre and Price, *J. Amer. Chem. Soc.*, 1956, **78**, 3432.

XUM

TABLE 2. *Comparison of calculated and experimental degrees of polymerization (reactions with no dioxan added, carried to completion).*

	At 93°				At 70°					
ν_0 *	114·1	54·6	30·9	8·26	126·6	54·3	52·1	36·6	35·3	18·8
ν	29	22	16·5	6·9	45	34	29	26	24	15·4

* From eqn. (1), $\nu_0 = [C_3H_6O]_0/([CH_3{\cdot}OH]_0 + [CH_3{\cdot}ONa]_0)$.

DISCUSSION

The general pattern of the kinetic results has been discussed above, and shown to be consistent with the postulated nature of the polymerization. Kinetic measurements in solution were made at only a single temperature, but from the runs in absence of solvent recorded in Table 1, the energy of activation is estimated as 17·4 kcal. mole^{-1}, very similar to the value (17·8) reported in Part II [1] for ethylene oxide. The A factor is $\sim 10^7$ l. mole^{-1} sec.$^{-1}$, which is a power of ten less than for ethylene oxide. This comparison suggests that the lower polymerisability of propylene oxide than of ethylene oxide arises from a greater steric restriction of the propagation reaction. More precise results would be needed to confirm this.

Although the observed kinetic behaviour can be explained in terms of a simple polymerization mechanism, study of the products shows that the reaction must be more complex. It was reported by St. Pierre and Price [6] that polypropylene oxides obtained by base-catalysed polymerization contain unsaturated centres. Infrared examination of our polymers confirms this. Moreover, Table 2 reveals a considerable discrepancy between the observed molecular weights and those calculated on the basis of equation (1). In a preliminary report on this work [7] it was suggested that both these features arise from a transfer reaction in which the propagating ion abstracts a proton from a molecule of monomer, which then acts as initiator for a new (unsaturated) chain. This suggestion was illustrated by the equations:

$$RO^- + CH_2(O)CHMe \longrightarrow ROH + CH_2{=}CMe{\cdot}O^-$$

$$CH_2{=}CHMe{\cdot}O^- + n\,CH_2(O)CHMe \longrightarrow CH_2{=}CMe{\cdot}[O{\cdot}CH_2{\cdot}CHMe]_n{\cdot}O^-$$

Simons and Verbanc [8] recently put forward the same type of reaction, but pointed out that the unsaturation is most simply interpreted if the transfer reaction involves mainly the methyl group: the end group of the new chain would then be allylic ($CH_2{=}CH{\cdot}CH_2{\cdot}O^-$). They further suggest that the propenyl end groups also observed arise by a subsequent base-catalysed isomerization. Present evidence does not seem adequate to resolve the fine details. If we write the propagation and transfer reactions as:

$$P + M \longrightarrow P \text{ (rate constant } k)$$
$$P + M \longrightarrow P' + A \text{ (rate constant } \alpha k)$$

the products of the transfer are an alcohol (A) and a new type of alkoxide ion (P′). The latter will then participate in the general ion–alcohol equilibria, according to its acid strength, and can also propagate new chains. No simple exact analysis of the consequences of this step is possible, but an approximate treatment is readily given if we ignore * differences of reactivity and basicity between P′ and P. The transfer reaction has then no effect on the rate of polymerization but introduces one additional potential chain-initiator. Following the argument of Part II we assume proton exchange between ion and alcohol to

[7] Gee, *Chem. and Ind.*, 1959, 678.
[8] Simons and Verbanc, *J. Polymer Sci.*, 1960, **44**, 303.

XUM

be rapid. Let C_0 = initial concn. of NaOMe, n = concentration of chains (initially n_0), and [M] = concentration of monomer (initially $[M]_0$), then

$$-d[M]/dt = (1 + \alpha)k[M]C_0$$
$$dn/dt = \alpha k[M]C_0$$

whence,
$$n = n_0 + \frac{\alpha}{1 + \alpha}([M]_0 - [M]). \quad (3)$$

The number-average degree of polymerization, ν, is given † by $\nu = ([M]_0 - [M])/n$. In the absence of transfer we should have found:

$$\nu_0 = ([M]_0 - [M])/n_0$$

whence
$$\frac{1}{\nu} = \frac{1}{\nu_0} + \frac{\alpha}{1 + \alpha}. \quad (4)$$

The concentration of unsaturated chains is $(n - n_0)$; hence the ratio of double bonds to molecules of monomer polymerized will be

$$(n - n_0)/([M]_0 - [M]) = \alpha/(1 + \alpha). \quad (5)$$

Two conclusions follow from this analysis: (i) A plot of $1/\nu$ against $1/\nu_0$ should be linear, with an extrapolated value $\alpha/(1 + \alpha)$. (ii) The unsaturation (equiv. per g. of polymer)

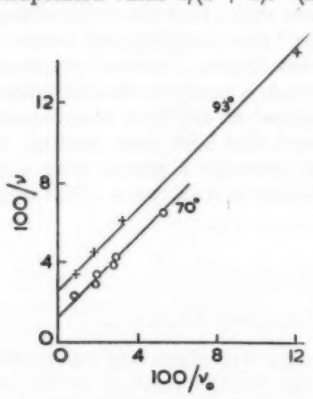


FIG. 2. *Observed (ν) and calculated (ν_0) degrees of polymerization.*

should be independent of the degree of polymerization, and a function only of the polymerization temperature. The first conclusion is borne out by Fig. 2, in which the values in Table 2 are plotted. The lines drawn are of unit slope, as suggested by equation (4); their intercepts give $\alpha = 0{\cdot}013_0$ at 70° and $0{\cdot}026_9$ at 93°. Comparison of these two figures shows that the transfer reaction requires an activation energy greater by 7·7 kcal. mole^{-1} than that for propagation, and is thus approximately 25 kcal. mole^{-1}.

The second conclusion cannot be checked from our own work, but appears to be at variance with the unsaturation values reported by Simons and Verbanc.[8] Although these authors recognize that their experimental procedure is open to criticism on the grounds that propenyl ether is probably destroyed, they seem to show that the unsaturation increases during polymerization. The explanation offered by Simons and Verbanc, which requires the propagation to involve alcohol as well as base and epoxide, seems to us unlikely and is not supported by our kinetic work. A very similar effect could possibly

* These may in any case tend to compensate each other (cf. Part II).

† This neglects consumption of monomer as a chain initiator. A more precise analysis does not materially affect the conclusions drawn.

arise from the change in the medium during the continued addition of monomer in the technique used by these authors. We have shown the importance of medium in modifying reaction rates; if this effect operated differentially between the competing reactions of propagation and transfer, it would cause α to vary during the reaction. Our own measurements would be less subject to this effect since we have used a closed reaction system.

There are at least two other ways in which an apparently low unsaturation in the early stages could arise, consistently with our general mechanism: (i) If the proton transfer produces the ion $CH_2{=}CH{\cdot}CH_2{\cdot}O^-$ the rate of incorporation of this in a new chain will be influenced both by its reactivity, relative to that of the other ions present, and by its participation in acid–base equilibrium. (ii) The unsaturated polymer formed will always have a molecular weight lower than the average. We have shown qualitatively that under molecular-still conditions a small fraction, of enhanced unsaturation, could be distilled from a polymer of average molecular weight 500. Such material would be water-soluble and would therefore be partially lost in the procedure used by Simons and Verbanc for recovery of their polymer. The proportion lost in this way would naturally be highest in polymers of low average degree of polymerization.

We conclude that, although considerably more work would be needed to establish the precise nature of the polymer formed, the simple mechanisms we have put forward are in agreement with the essential facts.

THE UNIVERSITY, MANCHESTER, 13. [*Received, December 23rd,* 1960.]

---

848. *The Interaction of Decalin and Isobutyryl Chloride–Aluminium Chloride.*

By M. S. AHMAD and G. BADDELEY.

This reaction, in the absence of an excess of the metal halide and under the mildest conditions compatible with a convenient rate, is shown to give 10β-2′-methylpropenyl-*trans*-decalin 1β,1′-oxide (I) in about 40% yield. Several novel decalin derivatives are provided by oxidation of compound (I) with peracid.

PREVIOUS investigations [1,2] having shown the primary product of interaction of decalin and acetyl chloride–aluminium chloride to be 1β,1′-epoxy-10β-vinyl-*trans*-decalin, we wished to know whether other fatty acid chlorides having at least one hydrogen atom on the α-carbon atom would react similarly. We have used propionyl and isobutyryl chloride and this paper is concerned with the product given by the latter reagent. In a typical experiment, decalin (1·8 mol.) reacted in the cold (<10°) with aluminium chloride (2·0 mol.) and isobutyryl chloride (2·2 mol.) in ethylene dichloride, to give an oil, $C_{14}H_{22}O$ (0·40 mol.), b. p. 128—130°/10 mm., which was shown, as described below, to be the oxide (I), called below the vinyl ether. In accordance with the formulation (i) of the reaction, isobutyraldehyde was another product.

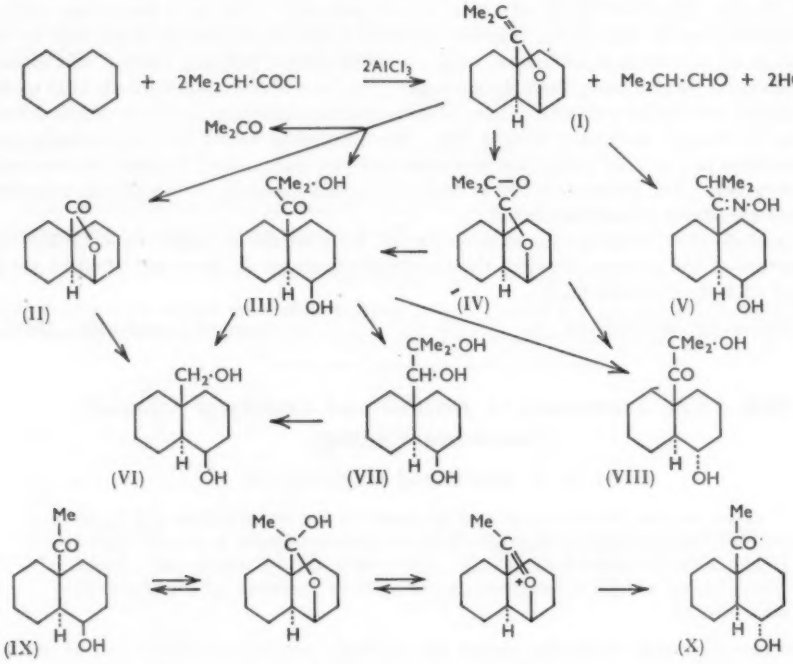
The vinyl ether (I) gave a deep colour with tetranitromethane, decolorised bromine in carbon tetrachloride, reacted with 1 mol. of perbenzoic acid, and has a strong absorption band at 1695 cm.$^{-1}$ which is provided by the vinyl ether group and not by a carbonyl group since the compound is unreactive towards lithium aluminium hydride. As a vinyl ether, it is stable in alkali but not in acid, and it slowly combines with hydroxylamine in neutral and weakly acid media to give an oxime, $C_{14}H_{25}O_2N$, which, doubtless, is correctly represented by (V). Ozonolysis of the vinyl ether in ethyl acetate gave acetone and the lactone [1] (II) which, for identification, was reduced to 10β-hydroxymethyl-*trans*-1β-decalol (VI) which also has previously been described.[1] These results described suffice to

[1] Baddeley, Heaton, and Rasburn, *J.*, 1960, 4713.
[2] Baddeley, Heaton, and Rasburn, *J.*, 1961, 3828.

XUM

show the vinyl ether (I) to be a major product of the interaction with which this paper is concerned. Below we describe other products of oxidation of the vinyl ether.

The ozonolysis described above gave also a solid, $C_{14}H_{24}O_3$, which was obtained again when the vinyl ether reacted with peracids. As shown below, it is the dihydroxy-ketone (III). (*a*) Its infrared absorption spectrum has bands at 3623 and 3448 (OH) cm.$^{-1}$ and another at 1678 (C=O) cm.$^{-1}$ which disappears when the compound is reduced with lithium



aluminium hydride to a triol, $C_{14}H_{26}O_3$ (VII). (*b*) Although it does not react with periodic acid, it is oxidised by lead tetra-acetate to acetone and a compound, probably the lactone (II), which with lithium aluminium hydride gave the known diol (VI). With lead tetra-acetate, the triol (VII) gave acetone and an oil, probably 10β-formyl-*trans*-1β-decalol, which was reduced to the diol (VI). Compound (III) was most readily obtained by careful hydrolysis of the acetal (IV) produced by interaction of the vinyl ether and perbenzoic acid. Less careful hydrolysis of the acetal gave an isomer of (III), namely, the 1α-alcohol (VIII). This has infrared absorption bands at 1678 (C=O), 3460, and 3311 (OH) cm.$^{-1}$, gave acetone when oxidised with lead tetra-acetate, and was reduced with lithium aluminium hydride to a triol, m. p. 130—131°. The isomerisation (III ⟶ VIII) is readily effected by dilute acid and is analogous to the previously reported isomerisation of (IX) to (X).[2] After five hours at room temperature, a mixture of the vinyl ether and peracetic acid gave compound (III), whereas after two days and in the presence of added glacial acetic acid compound (VIII) (mainly as a monoacetyl derivative) was obtained.

Experimental

1β,1′-*Epoxy*-10β-2′-*methylpropenyl*-trans-*decalin* (I).—Decalin (55 g.) was added to a homogeneous solution of aluminium chloride (107 g.) and isobutyryl chloride (94 g.) in ethylene chloride (300 ml.) at 0°. After being kept overnight at 0°, the mixture was poured slowly on

a stirred mixture of ice and dilute hydrochloric acid, and the organic layer was separated, washed with water, dried (K_2CO_3), and distilled. Decalin (24 g.), b. p. <90°/10 mm., was recovered and the required *compound* (37 g.), was obtained as an oil, b. p. 128—130°/10 mm. (Found: C, 81·2; H, 10·6. $C_{14}H_{22}O$ requires C, 81·5; H, 10·7%). A portion of the aqueous layer was heated and evolved isobutyraldehyde (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 187°).

Oxime (V) *of* 10β-*Isobutyryl*-trans-1β-*decalol*.—The above vinyl ether reacted slowly (20 hr. on the steam bath) with hydroxylamine in neutral or weakly acidic aqueous ethanol to give the required *oxime* which separated as needles, m. p. 171—172° (Found: C, 70·4; H, 10·5; N, 6·0. $C_{14}H_{25}NO_2$ requires C, 70·3; H, 10·4; N, 5·9%).

Ozonolysis of the Vinyl Ether.—This compound (10·0 g.) in ethyl acetate (80 ml.) gave, with ozone, a greenish-yellow solution which was heated with water (10 ml.) on the steam bath. Acetone (2,4-dinitrophenylhydrozone, m. p. and mixed m. p. 125—126°) was evolved and the residue was extracted with ether. The ether extract was washed with sodium hydrogen carbonate solution and dried (K_2CO_3) and gave a solid (1·5 g.), m. p. and mixed m. p. 145—146°, shown below to be 10β-(2-hydroxy-2-methylpropionyl)-*trans*-1β-decalol (III), and an oil (6·2 g.), b. p. 145—150°/15 mm. This oil was shown to be the lactone (II) of 1β-hydroxy-*trans*-decalin-1β-carboxylic acid by (*a*) its infrared absorption spectrum which was compared with that of an authentic sample [1] and (*b*) its reduction with lithium aluminium hydride to 10β-hydroxymethyl-*trans*-1β-decalol [1] (VI), m. p. and mixed m. p. 110°.

The Vinyl Ether and Perbenzoic Acid.—A solution of these reactants (2·0 and 1·40 g., respectively) in chloroform (40 ml.) was kept at room temperature for 2 hr. and worked up in the usual way to give a syrup, presumably the acetal (IV), which was devided into two equal samples. A solution of one sample in aqueous acetone (12 ml.) was acidified with two drops of glacial acetic acid and stored at room temperature for 3 days. It gave the *dihydroxy-ketone* (III) which separated from light petroleum–ethyl acetate in needles (0·48 g.), m. p. 145—146° (Found: C, 70·2; H, 9·8. $C_{14}H_{24}O_3$ requires C, 70·0; H, 10·0%). A solution of the other sample in aqueous acetone (20 ml.) was acidified by glacial acetic acid (5 drops) and heated for 6 hr. on the steam bath. It gave the isomer 10β-(2-*hydroxy*-2-*methylpropionyl*)-trans-1α-*decalol* (VIII), which separated from light petroleum–ethyl acetate in needles (0·40 g.), m. p. 165—166° (Found: C, 69·8; H, 9·8%). In another experiment, a solution of the vinyl ether (1·0 g.) and perbenzoic acid (1·0 g., 1·5 mol.) in chloroform (26 ml.) was kept for a day: only one mol. of the oxidant was consumed. The resulting acetal (0·8 g.) was isolated as a viscous oil and was heated with several drops of 2N-sulphuric acid in dioxan (15 ml.) and water (2 ml.) at 100° for 2 hr.; it gave compound (VIII), m. p. and mixed m. p. 165—166°.

A solution of compound (III) (0·10 g.) and lead tetra-acetate (0·30 g.) in benzene (15 ml.) was kept for 2 days at room temperature and gave acetone (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 125—126°), and an oil which with lithium aluminium hydride gave the diol (VI), m. p. and mixed m. p. 109—110°. Similar oxidation of compound (VIII) also gave acetone. Reduction of compound (III) (0·40 g.) with lithium aluminium hydride (0·250 g.) in ether (100 ml.) gave the 10β-1,2-*dihydroxy*-2-*methylpropyl*)-trans-1β-*decalol* (VII) (0·33 g.) as needles, m. p. 136—137°, from light petroleum–ethyl acetate (Found: C, 69·3; H, 10·8. $C_{14}H_{26}O_3$ requires C, 69·4; H, 10·7%). When oxidised with lead tetra-acetate in benzene it gave acetone and an oil which with lithium aluminium hydride gave the diol (VI). Reduction of compound (VIII) (0·07 g.) with lithium aluminium hydride (0·15 g.) in ether (50 ml.) gave the 1α-*triol*, m. p. 130—131° (55 mg.) (Found: C, 69·4; H, 10·8%), which separated from light petroleum–ethyl acetate in minute prisms which depressed the m. p. of its isomer (VII) on admixture.

The Epimerisation (III ⟶ VIII).—Compound (III) (100 mg.) in a little ethyl acetate was shaken with water (10 ml.) to which glacial acetic acid (5 drops) had been added. After 5 hr. at 100°, the mixture was cooled and the solid was separated and recrystallised from light petroleum–ethyl acetate; compound (VIII), m. p. and mixed m. p. 165—166°, was obtained.

The Vinyl Ether and Peracetic Acid.—A homogeneous mixture of the vinyl ether (2·0 g.), chloroform (10 ml.), glacial acetic acid (0·5 ml.), and 40% peracetic acid (7 ml.) was kept at 0° for 5 hr. It gave compound (III) (0·9 g.), m. p. and mixed m. p. 145—146°. A mixture of the vinyl ether (1·0 g.), chloroform (5 ml.), glacial acetic acid (5 ml.), and 40% peracetic acid (2·5 ml.) was kept at room temperature for 2 days and gave a product from which compound (VIII) (0·15 g.), m. p. and mixed m. p. 165—166°, and its *monoacetate* (0·40 g.), m. p. 122—123°

XUM

(from light petroleum–ethyl acetate) (Found: C, 68·1; H, 9·6. $C_{16}H_{26}O_4$ requires C, 68·1; H, 9·2%), were isolated. Compound (VIII) and its monoacetate gave the same triol, $C_{14}H_{26}O_3$, m. p. 130—131°, when reduced with lithium aluminium hydride.

THE MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY,
MANCHESTER.

[*Received, February 30th*, 1961.]

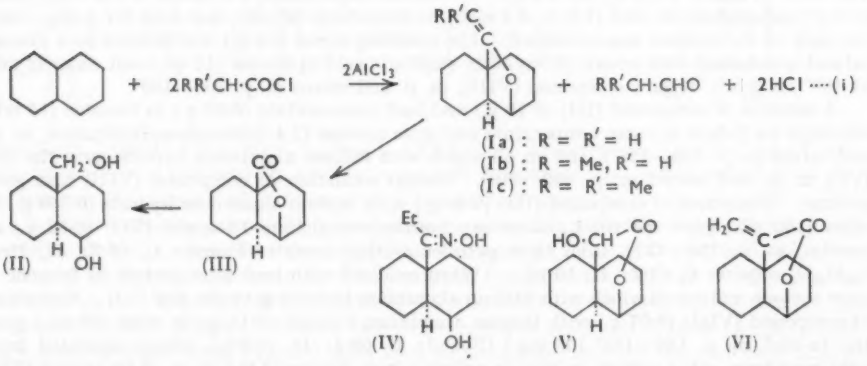
---

849. *The Interaction of Decalin, Propionyl Chloride, and Aluminium Chloride.*

By G. BADDELEY and B. G. HEATON.

A product of this reaction gave acetaldehyde and the lactone (III) of 4β-hydroxy-*trans*-decalin-9β-carboxylic acid on ozonolysis; it is, therefore, the vinyl ether (Ib). Some of its properties are compared with those of the previously reported [1,2] vinyl ethers (Ia and c). Like them it was obtained in 40% yield.

THE reaction (i) formulated below, in which the interaction of decalin and a Friedel–Crafts acylating agent gives a vinyl ether (I), was shown to occur when R = R′ = H or Me; we are now concerned to show that it occurs also when R = Me, R′ = H, and to compare several properties of the products (Ib and c) with those of (Ia). By using propionyl chloride, the ether (Ib) was obtained in about the same yield (40% based on the amount of aluminium chloride) as was reported [1,2] for (Ia and c). The structure of the product was easily determined: the product was an oil, $C_{13}H_{22}O$, which decolorised bromine in carbon tetrachloride, was not reduced with lithium aluminium hydride, was stable in alkali, combined with hydroxylamine in neutral or weakly acidic media to give an oxime, $C_{13}H_{23}O_2N$ (IV), and on ozonolysis in hexane gave acetaldehyde and the lactone (III)



which was identified by its infrared spectrum and by its reduction by lithium aluminium hydride to 10β-hydroxymethyl-*trans*-1β-decalol. The vinyl ether (Ib) can be either of two geometrical isomers and we assume that out product is the less crowded one, the methyl group being *trans* to the decalin portion with respect to the ethylenic double bond.

The three vinyl ethers (Ia, b, and c) behaved differently towards an excess of perbenzoic acid: (Ic) reacted with only one mol. of the peracid to give a viscous oil which was probably the acetal;* (Ib) rapidly consumed this amount of peracid and a third more in 67 hours,

* Cf. compound (IV) of preceding paper.

[1] Baddeley, Heaton, and Rasburn, *J.*, 1960, 4713.
[2] Ahmad and Baddeley, preceding paper.

to give a mixture from which a small amount of a solid, $C_{13}H_{18}O_2$, was isolated; and (Ia) consumed about 2 mol. of the peracid in 24 hours, to give the hydroxy-lactone (V), the corresponding keto-lactone, and a little of the γ-lactone (III). The solid, $C_{13}H_{18}O_2$, rapidly decolorised bromine in carbon tetrachloride, gave a brown colour on addition to tetranitromethane, has strong absorption bands at 1733 and 917 cm.$^{-1}$ (δ-lactone), and has a vinyl group (see VI).

Towards hydroxylamine in weakly acidic media, the ether (Ic) is far less reactive, possibly as a consequence of steric hindrance, than the other two.

Infrared absorption by the vinyl ether groups in (Ia, b, and c) is at 1667, 1698, and 1695 cm.$^{-1}$, respectively. The strong band at 793 [·O·C(:CH_2)·] cm.$^{-1}$ in the spectrum of (Ia) is not given by compounds (Ib and c). The stretching vibration of the C–H bonds of the ethylenic groups in (Ia and b) provides weak absorption at 3110 and 3086 cm.$^{-1}$, respectively, while (Ic), understandably, does not absorb in this region.

Experimental

1β,1′-*Epoxy*-10β-*prop*-1′-*enyl*-trans-*decalin* (Ib).—Decalin (69 g.) was added to a homogeneous solution of propionyl chloride (102 g.) and aluminium chloride (133 g.) in ethylene chloride (300 ml.) at 10°. The mixture was kept overnight at this temperature and then slowly added to a stirred mixture of ice and water. The organic layer was separated, washed with water, dried (K_2CO_3), and distilled; it gave decalin (25 g.), b. p. 70—80°/17 mm. and the required *compound* (42 g.), b. p. 118—122°/17 mm., n_D^{25} 1·5033 (Found: C, 80·8; H, 10·4. $C_{13}H_{20}O$ requires C, 81·2; H, 10·4%), $\nu_{max.}$ at 1698, 1100, 1010, and 912 cm.$^{-1}$.

The oxime of 10β-*Propionyl*-trans-1β-*decalol* (IV).—The above vinyl ether (0·9 g.) with hydroxylamine hydrochloride (2·5 g.) and potassium hydroxide (1·0 g.) in 50% aqueous ethanol (20 ml.) was heated on the steam bath and then made homogeneous by addition of ethanol (7 ml.). After 15 min., the mixture was cooled and the required *oxime* (0·77 g.) separated as prisms, m. p. 172—174° (Found: C, 69·7; H, 10·5; N, 6·2. $C_{13}H_{23}NO_2$ requires C, 69·3; H, 10·2; N, 6·2%).

Ozonolysis of the Vinyl Ether.—This compound (10 g.) was ozonised in n-hexane at 4° and evolved acetaldehyde (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 159—161°), when heated with water (20 ml.) on the steam bath. The residue gave an oil (1·0 g.), b. p. 143—148°/16 mm., and the lactone (III) of 4β-hydroxy-*trans*-decalin-9-carboxylic acid (5·3 g.) which was identified by its infrared absorption spectrum and by reduction of a sample (1·0 g.) with lithium aluminium hydride in ether (80 ml.) to 10β-hydroxymethyl-*trans*-1β-decalol (II) (0·8 g.), m. p. and mixed m. p. 110°.

The Vinyl Ether and Perbenzoic Acid.—These reactants (0·31 and 0·66 g., respectively) in chloroform (40 ml.) at 0° provided a rapid reaction which consumed 1 mol. of peracid in a few minutes and a further 0·33 mol. in the following 67 hr. A mixture of the vinyl ether (10 g.) and perbenzoic acid (8·6 g.) in chloroform (380 ml.) was kept at 0° for 2·5 hr. Calcium hydroxide (20 g.) was then added, the mixture was filtered, and the filtrate was distilled at 0·55 mm., three fractions being collected: b. p. 75—102° (2·9 g.); b. p. 102—115° (2·4 g.); and b. p. 115—118° (2·0 g.). The last fraction solidified and crystallised from light petroleum in prisms, m. p. 192—194° (Found: C, 76·1; H, 8·7. Calc. for $C_{13}H_{18}O_2$: C, 75·7; H, 8·7%).

Manchester College of Science and Technology,
Manchester, 1.

[*Received, January 30th*, 1961.]

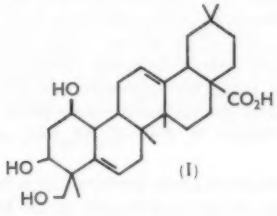
XUM

850. *The Structure of Bassic Acid.*[1]

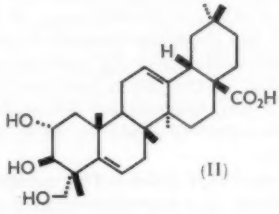
By T. J. King and J. P. Yardley.

The conversion of bassic acid and of anhydroterminolic acid into a common derivative by periodate oxidation established the structure of the former as 2,3,23-trihydroxyolea-5,12-dien-28-oic acid. Methyl 23-deoxybassate readily formed an isopropylidene derivative, showing that the 2- and the 3-hydroxyl group are in *cis*-relation. Borohydride reduction of a derived *vic*-diketone, regenerating methyl deoxybassate, established the complete formula of bassic acid as 2β,3β,23-trihydroxyolea-5,12-dien-28-oic acid.

Bassic acid is widely distributed as glycosides in the saponins of many plants of the order *Sapotacea*[2] and was first isolated in a pure form and investigated in detail by Heywood, Kon, and Ware,[3] who classed it as a trihydroxydienoic acid of the triterpene series and assigned to it the structure (I). This work has recently been summarised[4] and it has been pointed out that the experimental results on which this structure was based could be re-interpreted and did not exclude a 2,3,23(or 24)-trihydroxy-structure. It was further pointed out that no conclusive reasons for allocating an oleanane skeleton to bassic acid had been put forward. We also had been unconvinced of the validity of Kon's arguments since we became interested in bassic acid after its isolation from *Mimusops heckelii* (Makoré) in this laboratory,[5] and we have reinvestigated the chemistry of the acid.



(I)



(II)

From the beginning our efforts were turned towards the conversion of bassic acid and anhydroterminolic acid[6] (II) into a common derivative. The latter is isomeric with bassic acid and has both double bonds in the same position as suggested for the double bonds of that acid.

No difficulty was found in obtaining bassic acid from commercially available Mowrah meal. The best results came from the use of meal with a low fat content (*ca.* 1—2%), when a preliminary extraction with light petroleum was unnecessary. Percolation of such meal at 40° with 80% ethanol gave an extract which was readily hydrolysed by acid, the bassic acid produced being most easily purified through the sodium salt. In this way yields of about 0·5% of the meal may be obtained.

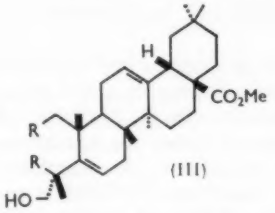
Much of our earlier work was based on the erroneous assumption that bassic acid did not react with periodate and thus lacked a *vic*-glycol function. Such a result was reported by the earlier workers and was, early in our own work, confirmed independently by both the present authors. However, our inability to reconcile many of our experimental findings with the 1,3-arrangement of the secondary hydroxyl groups in bassic acid led us to repeat the periodate oxidation which was then successful. We are unable to explain the earlier failures.

[1] For a preliminary communication see King and Yardley, *Proc. Chem. Soc.*, 1959, 393.
[2] Heywood and Kon, *J.*, 1940, 713.
[3] Heywood, Kon, and Ware, *J.*, 1939, 1124.
[4] Simonsen and Ross, "The Terpenes," Cambridge Univ. Press, 1957, Vol. V, pp. 139—147.
[5] King, Baker, and King, *J.*, 1955, 1338.
[6] King and King, *J.*, 1956, 4469.

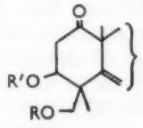
XUM

The product of periodate fission of methyl bassate was crystalline and a similar degradation of methyl anhydroterminolate gave an identical product which must have structure (III; R = CHO). The identity was further confirmed by comparison of the triols (III; R = CH_2·OH) formed by borohydride reduction of both specimens of the dialdehyde. This result established the structure, including the stereochemistry, of bassic acid with the exception of the configuration of the secondary hydroxyl groups. The α-(hydroxymethyl)-carbonyl nature of the fission product was confirmed when alkali afforded formaldehyde. The dialdehyde which would be the other product of this reverse aldol reaction failed to crystallise and presumably had undergone further base-catalysed reactions.

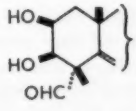
The highly crystalline isopropylidene derivative of methyl bassate, and its oxidation to the corresponding dehydro-derivative, were described by the earlier workers [2,3] who assigned to it the partial structure (IV; R + R′ = Me_2C<). We repeated this preparation with the aim of removing the carbonyl-oxygen atom. The chromic oxide–sulphuric acid–acetone [7] reagent was found to be greatly superior in this preparation to other common oxidising agents, *e.g.*, chromic oxide in acetic acid or pyridine, or acetone–aluminium t-butoxide. The derived dihydroxy-compound was stable to alkali, a fact which we found incompatible with its formulation as (IV; R = R′ = H) which would be expected



(III)



(IV)



(V)

to be dehydrated under these conditions. Methyl dehydroisopropylidenebassate was readily converted into methyl deoxybassate by a modified Huang-Minlon reduction of its hydrazone followed by acid hydrolysis and re-esterification. Standard Huang-Minlon conditions resulted only in partial removal of oxygen and the vigorous conditions described by Barton, Ives, and Thomas [8] gave low yields. The realisation that methyl dehydrobassate is an aldehyde (partial structure V) initially followed from the failure of repeated attempts to isolate formaldehyde from pyrolysis of methyl deoxybassate with copper bronze. This reaction, in the triterpene series, is regarded as characteristic of a 1,3-secondary-primary glycol and is given by methyl bassate.[3] The result showed that the free hydroxyl group in methyl isopropylidenebassate must be part of the 1,3-glycol system and must almost certainly be the primary hydroxyl group. This conclusion was confirmed by a study of the nuclear magnetic resonance spectrum of methyl dehydroisopropylidenebassate and of its semicarbazone. The aldehyde shows a singlet peak with τ 1·04, a higher value than usual for an aldehyde (*ca.* 0·35) but not attributable to any other than an aldehydic proton. The high value has stereochemical implications because the τ values for the aldehyde protons of the fully substituted equatorial aldehyde vinhatical [8] and its axial epimer, vouacapenal,[9] are 0·77 and 0·23 respectively. The presence of a singlet (τ 3·01) in the spectrum of the semicarbazone confirmed the above conclusions.[10]

In the light of present knowledge these results mean that the isopropylidene group in methyl isopropylidenebassate must bridge the 2,3-positions, and thus methyl deoxybassate must be a *vic*-glycol. Its fission by periodate confirmed this conclusion. Of the four possible arrangements of the hydroxy-groups only two would easily give an isopropylidene

[7] Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39.
[8] Barton, Ives, and Thomas, *J.*, 1955, 2056.
[9] Godson, King, and King, *J.*, 1955, 1117.
[10] Curtin, Gourse, Richardson, and Rinehart, jun., *J. Org. Chem.*, 1959, **24**, 93.

derivative, namely, the *cis*-αα- and the *cis*-ββ-glycols.[11] It has been pointed [12] out that no 2α,3α-glycol of the steroid or triterpene field occurs in Nature, so the presumption would be that bassic acid has the 2β,3β-configuration. Confirmation of this was sought by borohydride reduction of a derived 2,3-diketone, borohydride reduction of both 2- and 3-ketones in steroids and triterpenes being known to produce predominantly β-alcohols.[13] Methyl deoxybassate itself failed to afford a pure product on oxidation, but the bromo-lactone obtained from deoxybassic acid was oxidised readily by chromic oxide in acetic acid to a yellow crystalline compound having the spectral characteristics of a non-enolised *vic*-diketone and affording a quinoxaline with *o*-phenylenediamine. The un-enolised nature of this diketone is in marked contrast with that of the 4-demethyl-2,3-dione derivable [14] from hederagenin, and also with those members of the cucurbitacin group having the appropriate oxidation state.[15]

Professor Ourisson of Strasbourg has interested himself in this anomaly and tells us that the un-enolised nature of the diketone is due to its preparation under acid conditions and to its very slow rate of enolisation in neutral solutions. After brief treatment with alkali the expected diosphenol structure can be demonstrated by the positive ferric reaction and by ultraviolet and infrared absorption.

Borohydride reduction of the yellow diketone readily regenerated deoxybassic bromo-lactone, characterised by its diacetate and by reduction and methylation to methyl deoxybassate.

Djerassi and his co-workers [12,16] have used the rate of cleavage by lead tetra-acetate to determine the stereochemistry of 2,3-diols of both steroidal sapogenins and triterpenes, *e.g.*, medicagenic acid (2β,3β-diol) and arjunolic and asiatic acid (2α,2β-diols). A good determination of the rate of cleavage of methyl bassate under the conditions used by these authors was not possible because of the rapidity of the reaction, which gave an approximate rate constant of 500×10^{-3} l. mole^{-1} sec.$^{-1}$. This is so much larger than that of any previously measured triterpene 2,3-glycol (medicagenic acid: $k = 31 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$) that it must be assumed that the presence of the 5,6-double bond has a marked accelerating affect on the fission, and it would clearly be unjustifiable to make stereochemical deductions from this result. It is relevant that the Δ^5-derivative (yuccagenin) of gitogenin is oxidised some 3·5 times faster than gitogenin itself.

Kon and his co-workers [2,3] reported the existence of two forms of methyl bassate, one obtained by esterification with diazomethane or dimethyl sulphate and alkali (the α-form), the other obtained by the use of methyl iodide and alkali [17] (the β-form). These were reported as forming different acetates but the same isopropylidene derivative, and to differ markedly in their response to catalytic hydrogenation. We have been unable to substantiate this claim and in all cases our methyl bassate has corresponded in its properties and those of its derivatives with those recorded for β-methyl bassate.

New derivatives of bassic acid that we have made during this investigation include methyl 11,13(18)-dehydrobassate, obtained by the action of selenium dioxide on methyl triacetylbassate and subsequent hydrolysis. The optical properties of this conjugated diene are characteristic, and its formation is further evidence for the derivation of bassic acid from oleanolic acid.[18] The ready formation of the bromo-lactone of both bassic and deoxybassic acid was also an early confirmation of the basic skeleton. Further, we were able to oxidise diacetyldeoxybassic bromo-lactone to a crystalline 1,2-epoxide (presumably

[11] Slates and Wendler, *Chem. and Ind.*, 1955, 167.
[12] Djerassi, Thomas, Livingston, and Thompson, *J. Amer. Chem. Soc.*, 1957, **79**, 5292.
[13] See, for instance, King, King, and White, *J.*, 1958, 2830; Dauben, Glanz, jun., Jiu, and Micheli, *J. Amer. Chem. Soc.*, 1956, **78**, 3752.
[14] Ruzicka, Jeger, and Norymberski, *Helv. Chim. Acta*, 1944, **27**, 1185.
[15] See, for instance, Enslin, Hugo, Norton, and Rivett, *J.*, 1960, 4779; Lavie and Shvo, *Chem. and Ind.*, 1959, 429.
[16] Djerassi and Ehrlich, *J. Org. Chem.*, 1954, **19**, 1351.
[17] van der Haar, *Rec. Trav. chim.*, 1929, **48**, 1155, 1166.
[18] Ruzicka and Jeger, *Helv. Chim. Acta*, 1942, **25**, 775; Barton and Holness, *J.*, 1952, 78.

XUM

the 5,6α-epoxide), thus affording the only conclusive chemical evidence for the existence of the second double bond in bassic acid. In a similar way to the corresponding derivative of anhydroterminolic lactone, epoxybassic bromo-lactone with hydrogen chloride gave a chlorohydrin which was inert to oxidation with chromic oxide and reconverted into the epoxide in warm pyridine.

Olea-5,12-diene-2,3,23,28-tetraol and -2,3,28-triol have also been prepared by reduction of, respectively, methyl bassate and methyl deoxybassate with lithium aluminium hydride.

Experimental

Nuclear magnetic resonance data were obtained with a Varian Associates instrument operating at 40 Mc./sec. in deuterochloroform. Optical rotations were measured, except where indicated, in chloroform solution at 20° and for the D-line.

Extraction of Mowrah Meal.—Mowrah meal (51 kg.; fat content 1·6%) was stirred with ethanol (80 l.) at 40° for 8 hr. The extract was recovered by decantation and the procedure was repeated with a further 80 l. of solvent. The combined extracts were concentrated to 8 l. and added with stirring to ether (20 l.). The saponin ("Mowrin") which separated as a viscous golden-brown gum was immediately dissolved in 60% ethanol (30 l.) and the solution, in 2·5 l. portions, was boiled for 6—8 hr. with a 1 : 1 mixture (120 c.c.) of concentrated hydrochloric and sulphuric acid. Bassic acid separated from the hot solution as a coarse sand-coloured powder (30—50 g.) which was washed repeatedly with boiling 80% aqueous ethanol. A cold suspension of the impure acid (30—50 g.) in cold 60% aqueous ethanol (*ca.* 1 l.) was made weakly alkaline (pH 9—10) with concentrated aqueous sodium hydroxide, and the filtered dark solution was treated with an excess of sodium hydroxide (30—40 g.) and, after addition of charcoal, was again filtered. It was then evaporated on a steam-bath until a test portion crystallised on cooling. The sodium bassate so obtained separated from aqueous methanol as colourless rods (yield 20—30 g.). The total yield from the extraction was 280 g.

The acid separated from an acidified solution of the sodium salt in gelatinous form and for further experiments the salt was converted directly, in 75% yield, into the methyl ester by reaction in aqueous methanol with dimethyl sulphate and 10% aqueous sodium hydroxide. The ester separated from aqueous methanol as the *hemihydrate*, m. p. 180—190°, [α] +58° (*c* 0·52) (Found: C, 73·0; H, 9·5. $C_{31}H_{48}O_5,\frac{1}{2}H_2O$ requires C, 73·0; H, 9·7%). The anhydrous ester was obtained by crystallisation from acetone and had m. p. 216—218° after sintering at 192° (Found: C, 74·2; H, 9·5. Calc. for $C_{31}H_{48}O_5$: C, 74·4; H, 9·7%). Heywood and Kon [1] give for β-methyl bassate, m. p. 216—217°, [α] +56°. The identity of our material with bassic acid was checked by the preparation of the following derivatives (published constants in parentheses): bromo-lactone,[2] m. p. 220° (220°); isopropylidene-bromo-lactone,[2] m. p. 205—207° (205—206°); methyl triacetylbassate,[2] m. p. 149—150° (148—149°); methyl isopropylidenebassate,[3] m. p. 206—208° (205—206°).

Oxidation of Methyl Bassate and Methyl Anhydroterminolate with Periodate.—(*a*) Methyl bassate (250 mg.) in ethanol was treated with aqueous *ca.* 0·25M-sodium metaperiodate (10 c.c.), and the volume adjusted to 100 c.c. with ethanol. The mixture was kept at room temperature in the dark and the excess of periodate was estimated in the usual way (in 20 c.c. portions) at various times. Appropriate blank determinations were made at each time and the following results, expressed as percentage oxidation of one *vic*-glycol unit, were obtained; 3 hr. 53%; 8 hr. 70%; 23 hr. 95%. (*b*) An alcoholic solution of methyl bassate (1 g. in 200 c.c.) mixed with aqueous sodium metaperiodate (1 g. in 20 c.c.) was set aside at room temperature in the dark for 48 hr. The mixture was poured into water. The precipitated *dialdehyde* (III; R = CHO) crystallised from aqueous methanol (charcoal) in prisms (630 mg.), m. p. 183° (decomp.), [α] +183° (*c* 0·78) (Found: C, 73·5; H, 8·95. $C_{31}H_{46}O_5,\frac{1}{2}H_2O$ requires C, 73·3; H, 9·3%).

Oxidation of methyl anhydroterminolate (1 g.) in the same way (*b*) gave a product (470 mg.), m. p. 183° (decomp.) undepressed by the product from methyl bassate, [α] +188° (*c* 0·53) (Found: C, 73·6; H, 9·1%). The infrared absorption of the two specimens was identical.

Both specimens of the aldehyde were reduced in pyridine–methanol with an excess of potassium borohydride and gave the *triol* (III; R = CH_2·OH), rods (from methanol), m. p. 216°, [α] +88° (*c* 1·21) (Found: C, 74·0; H, 9·8. $C_{31}H_{50}O_5$ requires C, 74·1; H, 10·0%).

Alkaline Decomposition of the Dialdehyde.—The dialdehyde (200 mg.) in 3 : 7 v/v aqueous methanol (100 c.c.) containing potassium hydroxide (4 g.) was set aside overnight at room

temperature. The solution was made acid to Congo Red and distilled. Dimedone (70 mg.) was added to the distillate and after 30 min. the solution was concentrated to 20 c.c.; needles of the formaldehyde–dimedone compound (7·4 mg.) separated. It was identified by m. p. and mixed m. p. No crystalline compound could be isolated corresponding to the major fragment of the molecule.

Methyl Dehydroisopropylidenebassate.—A stirred suspension of methyl isopropylidenebassate (6·8 g.) in pure acetone (300 c.c.) was treated dropwise at 0—5° during 1 hr. with 6·3 c.c. of a solution prepared from chromic oxide (3 g.) concentrated sulphuric acid (2·8 c.c.) and water (15 c.c.). After a further 30 min. the mixture was diluted to 1 l., and the product was washed with potassium carbonate solution and water and purified by passage of its solution in benzene down a short column of alumina. After removal of benzene and crystallisation of the residue from methanol, methyl dehydroisopropylidenebassate (5·2 g.) separated in prisms m. p. 181—183° (lit.,[2] m. p. 181—183°) (Found: C, 76·0; H, 9·2. Calc. for $C_{34}H_{50}O_5$: C, 75·8; H, 9·4%). The *hydrazone*, prepared in boiling ethanol, crystallised from methanol as rods, m. p. 184—186°, $[\alpha]$ +39° (*c* 0·96) (Found: C, 73·9; H, 9·5; N, 5·1. $C_{34}H_{52}N_2O_4$ requires C, 73·7; H, 9·4; N, 4·9%); the *semicarbazone hydrate* formed rods (from aqueous ethanol), m. p. 171—174°, $[\alpha]$ +23·5° (*c* 0·85) (Found: C, 68·7; H, 9·1; N, 6·7. $C_{35}H_{53}N_3O_5,H_2O$ requires C, 68·5; H, 9·0; N, 6·85%).

Methyl Dehydrobassate.—Hydrolysis of the above isopropylidene derivative in methanol containing a little hydrochloric acid gave the aldehyde as needles (from methanol), m. p. 201—202° (lit.,[2] m. p. 202—203·5°), unaffected by treatment with 5% ethanolic sodium hydroxide at room temperature overnight or at the b. p. for 1 hr. The *oxime* crystallised from methanol in needles, m. p. 220°, $[\alpha]$ +61° (*c* 0·44) (Found: C, 72·2; H, 9·4; N, 2·7. $C_{31}H_{47}NO_5$ requires C, 72·5; H, 9·2; N, 2·7%), and the *oxime diacetate* (prepared by use of acetic anhydride–pyridine) was prisms (from aqueous methanol), m. p. 140° (effervescence), $[\alpha]$ +64° (*c* 0·79) (Found: C, 70·4; H, 8·4; N, 2·2; Ac, 13·6. $C_{35}H_{51}NO_7$ requires C, 70·3; H, 8·6; N, 2·3; 2Ac, 14·6%).

Deoxybassic Acid.—A solution of sodium hydroxide (90 g.) and 100% hydrazine hydrate (40 c.c.) in ethylene glycol (1 l.) was distilled until it refluxed freely at 185°. Methyl dehydroisopropylidenebassate hydrazone (12 g.) was then added and the solution was boiled for 14 hr. and diluted with water. The crystalline precipitate in ethanol (250 c.c.) was treated at the b. p. with concentrated hydrochloric acid (2 c.c.) for 15 min., nearly pure *deoxybassic acid* (8·6 g.) rapidly separating. The very sparingly soluble acid was recrystallised for analysis from ethanol; it had m. p. 306—309° (decomp.), $[\alpha]$ +80° (*c* 1·09 in pyridine) (Found: C, 76·9; H, 9·9. $C_{30}H_{46}O_4$ requires C, 76·55; H, 9·85%). The *methyl ester* (prepared by use of diazomethane) crystallised from methanol in needles, m. p. 216—218°, $[\alpha]$ +69° (*c* 1·04) (Found: C, 76·9; H, 9·65; OMe, 7·3. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0; 1OMe, 6·4%). *Methyl deoxyisopropylidenebassate*, prepared in acetone containing a trace of hydrochloric acid, crystallised from acetone in thin prisms, m. p. 157—159°, $[\alpha]$ +51° (*c* 0·79) (Found: C, 77·6; H, 9·6. $C_{34}H_{52}O_4$ requires C, 77·8; H, 10·0%). The *methyl ester diacetate* (obtained by using acetic anhydride–pyridine) formed flat prisms, m. p. 109—111°, $[\alpha]$ +44·5° (*c* 0·99), from aqueous methanol (Found: C, 73·9; H, 9·1; Ac, 16·9. $C_{35}H_{52}O_6$ requires C, 73·9; H, 9·2; 2Ac, 15·2%). Under the conditions previously used the methyl ester consumed periodate corresponding to the presence of 91·5% of one *vic*-glycol unit in 42 hr.

Methyl deoxybassate failed to give formaldehyde when heated with activated copper bronze at 270—290° or in refluxing biphenyl. That methyl bassate afforded formaldehyde under these conditions [3] was confirmed.

Deoxybassic Bromo-lactone.—Bromine (1·6 g.) in acetic acid (25 c.c.) was added during 30 min. to a heated (100°) and stirred suspension of finely powdered deoxybassic acid (4 g.) in acetic acid (250 c.c.) containing sodium acetate (16 g.). After a further 10 min. nearly all the acid dissolved and the solution was filtered and poured into water containing a little sodium hydrogen sulphite. The precipitate crystallised from methanol (charcoal) to give the *bromo-lactone* as colourless needles, m. p. 236—250° (decomp.), $[\alpha]$ +77° (*c* 1·03) (Found: C, 65·7; H, 8·5; Br, 13·0. $C_{30}H_{45}BrO_4$ requires C, 65·6; H, 8·25; Br, 14·5%); light absorption (in ethanol) ε_{210} 1600; ε_{220} 370; $\nu_{max.}$ (in CCl_4) 1770 cm.$^{-1}$. The bromo-lactone was reconverted into deoxybassic acid by zinc dust in acetic acid at 100° for 2 hr. The *diacetate* (acetic anhydride–pyridine) formed plates (from aqueous methanol), m. p. 231—232° $[\alpha]$ +74° (*c* 0·65) (Found: C, 64·5; H, 8·0; Br, 11·2; Ac, 15·7. $C_{34}H_{49}BrO_6$ requires C, 64·4; H, 7·8; Br, 12·6; 2Ac, 13·6%). The

XUM

isopropylidene derivative did not separate when prepared in acetone–hydrochloric acid, but was precipitated when its solution was poured into dilute ammonia. From methanol or aqueous methanol it formed rods, m. p. 214°, [α] +48° (*c* 0·43) (Found: C, 67·4; H, 8·4; Br, 12·9. $C_{33}H_{49}BrO_4$ requires C, 67·2; H, 8·4; Br, 13·5%).

Oxidation of Deoxybassic Bromo-lactone.—To a stirred and cooled suspension of deoxybassic bromo-lactone (2·3 g.) in acetic acid–water–sulphuric acid (250 c.c.; 50 c.c.; 0·25 c.c. of concentrated acid) was added, during 1 hr., a solution of chromic oxide (1 g.) in acetic acid (35 c.c.). After a further 10 min. the excess of reagent was reduced with sodium hydrogen sulphite and the solution was poured into water. The precipitate crystallised from ethanol–chloroform, to give the *diketone* as small yellow prisms (1 g.), m. p. 224° (decomp.), [α] +80° (*c* 0·4) (Found: C, 65·5, 65·7; H, 7·9, 7·2. $C_{30}H_{41}BrO_4$ requires C, 66·0; H, 7·6%), $\lambda_{max.}$ (in $CHCl_3$) 274 (ε 420) and 420 (ε 22) mμ. The colour was not removed by charcoal or by chromatography on alumina, and the compound gave no colour with ferric chloride. It formed a *mono-2,4-dinitrophenylhydrazone*, pale yellow needles, m. p. 264° (decomp.) (Found: C, 59·7; H, 6·4; Br, 10·9; N, 7·5. $C_{36}H_{45}BrN_4O_7$ requires C, 59·6; H, 6·25; Br, 11·0; N, 7·7%), $\lambda_{max.}$ (in $CHCl_3$) 249 (ε 10,000) and 372 (ε 26,300) mμ. The *quinoxaline derivative* prepared with *o*-phenylenediamine in acetic acid crystallised from methanol–chloroform in buff-coloured rods, m. p. 238° (decomp.) (Found: C, 70·3; H, 7·5; N, 4·5. $C_{36}H_{45}BrN_2O_2$ requires C, 70·0; H, 7·65; N, 4·5%), $\lambda_{max.}$ (in $CHCl_3$) 239 (ε 31,700), 310 (inflexion, ε 7800), and 321 (ε 9900) mμ. Leonard and Mader [19] give for the quinoxaline from 3,3,6,6-tetramethylcyclohexane-1,2-dione $\lambda_{max.}$ 238 (ε 31,000), 310 (ε 7900), and 321 (ε 9800) mμ.

A pyridine–methanol solution of the diketone (300 mg.) with an excess of potassium borohydride overnight afforded 170 mg. of pure deoxybassic bromo-lactone. The identity of the product was confirmed by the preparation of the acetate and by reduction to deoxybassic acid characterised as its methyl ester. In each case identity was established by mixed m. p. and identity of infrared absorption.

Methyl 11,13(18)-*Dehydrobassate.*—Methyl triacetylbassate (300 mg.) was heated with selenium dioxide (300 mg.) in boiling acetic acid (30 c.c.) for 3 hr. The product precipitated with water was hydrolysed for ½ hr. with boiling 5% methanolic potassium hydroxide, and then water precipitated the *triene* (160 mg.) which crystallised from methanol in rods, m. p. 240—244°, [α] −195° (*c* 0·33) (Found: C, 74·4; H, 8·9. $C_{31}H_{46}O_5$ requires C, 74·7; H, 9·3%), $\lambda_{max.}$ (in EtOH) 243 (ε 24,650), 250 (ε 27,150), and 258 (ε 16,700) mμ.

Diacetylepoxydeoxybassic Bromo-lactone.—Diacetyldeoxybassic bromo-lactone (1 g.) in acetic acid (15 c.c.) was treated at 100° for 3 hr. with an excess of 30% hydrogen peroxide (0·7 c.c.). The *product* was isolated by dilution, and crystallised from methanol as plates (600 mg.), m. p. 230°, [α] +56° (*c* 0·71) (Found: C, 62·6; H, 7·4; Br, 11·9. $C_{34}H_{49}BrO_7$ requires C, 62·85; H, 7·6; Br, 12·5%).

2,3-*Diacetyl*-6-*chloro*-5-*hydroxydeoxybassic Bromo-lactone.*—The above epoxide (0·5 g.) was treated in chloroform with hydrogen chloride at room temperature for 1 hr. After removal of the solvent the residue crystallised from aqueous acetone, giving the chlorohydrin (0·27 g.) as thin rods, m. p. 238° (decomp.) (Found: C, 59·4; H, 7·3. $C_{34}H_{50}BrClO_7$ requires C, 59·5; H, 7·35%). The chlorohydrin reverted to the epoxide in warm pyridine and was recovered after treatment with an excess of chromic oxide in acetic acid–sulphuric acid at room temperature for 5 days.

Olea-5,12-*diene*-2,3,23,28-*tetraol.*—Methyl bassate (1 g.) was reduced in tetrahydrofuran (40 c.c.) with an excess of lithium aluminium hydride at the b. p. for 3 hr. Working up in the usual way gave the *tetra-ol* as prisms m. p. 216—219°, [α] +56° (*c* 0·33), from aqueous methanol or ethyl acetate (Found: C, 76·0; H, 10·0. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·2%).

Olea-5,12-*diene*-2,3,28-*triol.*—Methyl deoxybassate was reduced as in the previous experiment and gave the *triol* which crystallised from benzene as dense prisms, m. p. 179—181°, [α] +63° (*c* 0·68) (Found: C, 78·7; H, 10·1. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·3%).

Our thanks are offered to Messrs. Boots Pure Drug Co., Ltd., for supplying and carrying out the large-scale extraction of mowrah meal, and to Dr. L. M. Jackman for measuring and interpreting the nuclear magnetic resonance spectra.

Department of Chemistry, Nottingham University. [*Received, May 2nd,* 1961.]

[19] Leonard and Mader, *J. Amer. Chem. Soc.*, 1950, **72**, 5388.

XUM

851. *Polynitronaphthalenes. Part III.*[1,2] *A Quantitative Study of the Further Nitration of the Ten Dinitronaphthalenes.*

By E. R. Ward and C. D. Johnson.

A quantitative study has been made of the nitration in sulphuric–nitric acid, and in aqueous nitric acid alone, of all ten dinitronaphthalenes and of some trinitronaphthalenes. By the competition method 1- and 2-nitronaphthalene were found to be about equally reactive in nitration in sulphuric acid. The results are discussed in relation to current theories of aromatic nitration and good agreement has been found with theoretical predictions based on molecular-orbital theory.

For comparison, reaction of 1- and 2-nitronaphthalene with the brominium ion Br^+ has been investigated.

Naphthalene was first nitrated by Laurent as long ago as 1835 and its commercial development followed on Roussin's investigations into the properties of mono- and di-nitronaphthalenes (1861). Nevertheless, not until the completion of the present investigation was it possible to describe, even qualitatively, all the polynitronaphthalenes that can arise from the direct nitration of naphthalene in sulphuric acid. These are now given in the scheme.

Our systematic studies of the further nitration of polynitronaphthalenes are now complete, with quantitative results for the nitration of all ten dinitronaphthalenes (and of some trinitronaphthalenes) in nitric–sulphuric acid, and, in some cases, in nitric acid alone. These are summarised in Tables 1—4.

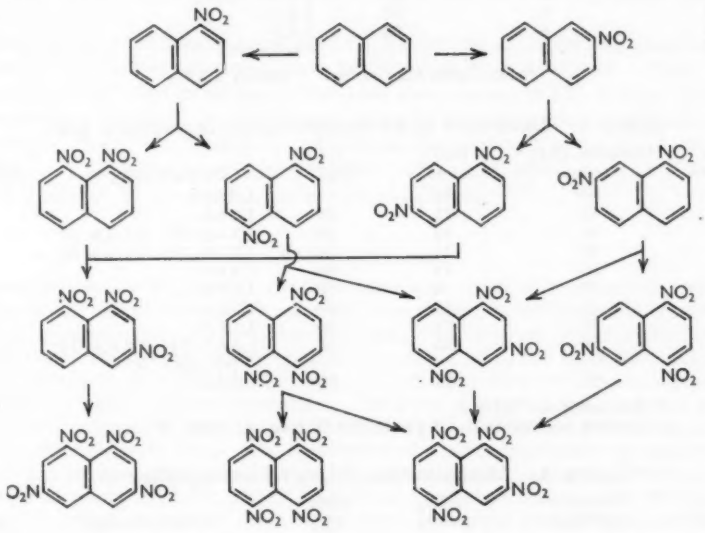
In confirmation of our previous work,[2] we have again found that for nitrations in aqueous nitric acid alone the amount of substitution in an α-position *peri* to an existing nitro-group is diminished, which we have suggested is due to increased reagent size in this medium.

In order to interpret more exactly the nitration of the polynitronaphthalenes we have made limited and preliminary studies of their relative reactivities by the competition method. Unfortunately difficulties in analysing the reaction products, except from the mononitronaphthalenes, enabled us to get only approximate values. 1- and 2-Nitronaphthalene were about equally reactive on nitration in either acetic anhydride or in sulphuric acid. For the dinitronaphthalenes relative reactivities were obtained which we considered sufficiently accurate to provide useful data and they have been published elsewhere.[3] It is hoped to make a much more detailed investigation based on the experience gained in these preliminary studies. However, it was found that 2,6- and 2,7-dinitronaphthalene are not the most reactive of the dinitronaphthalenes, as previously thought,[1] and that the difficulty in achieving mononitration only with these isomers may by due to the exceptional reactivity of the intermediate trinitronaphthalenes.

Bachman *et al.*[4] claimed that nitration of naphthalene by the boron trifluoride–nitrogen tetroxide complex in nitromethane at 80° produces a mixture of 1,5- and 1,8-dinitronaphthalene (products arising from 2-nitronaphthalene were not mentioned) in a ratio of *ca.* 1·7 : 1, in contrast to the usual ratio of 1 : 2 found for all other types of nitration. We have now nitrated 1-nitronaphthalene at −5° with Bachman's reagent and find an almost normal ratio of **39 : 61**, based on a quantitative yield of dinitronaphthalenes. Hence this type of nitration is not peculiar and no special explanation is required to interpret the results (cf. Ward *et al.*[2,5]).

[1] Part I, Hodgson and Ward, *J.*, 1946, 533.
[2] Part II, Ward, Johnson, and Day, *J.*, 1959, 487.
[3] Johnson, Thesis, London, 1960.
[4] Bachman, Feuer, Bluestein, and Vogt, *J. Amer. Chem. Soc.*, 1955, **77**, 6188; Bachman and Vogt, *ibid.*, 1958, **80**, 2381.
[5] Ward, *Chem. and Ind.*, 1956, 195.

Evidence for the dipolar effect of a nitro-group in aromatic electrophilic substitution [6] (leading to substitution *ortho* or *peri* to an existing nitro-group) has been previously limited to nitration studies, and so does not exclude the possibility that this effect is peculiar to nitration. We therefore investigated the bromination, in sulphuric acid, of 1- and 2-nitronaphthalene by the brominium ion Br^+, using the method of Derbyshire and Waters.[7] The brominium ion might be expected to behave somewhat similarly to the nitronium ion,



although of course steric requirements will differ. Complete analysis of the products by column chromatography could not be achieved. Infrared spectroscopic analysis of the product from 1-nitronaphthalene gave the composition as 1-bromo-5-nitronaphthalene, 60 ± 10%; 1-bromo-8-nitronaphthalene, 15 ± 10%; 1-nitronaphthalene, 15 ± 10%; and *ca.* 10% of other material (probably a dibromonitronaphthalene but not 1,4-dibromo-5-

TABLE 1. *Mononitration of dinitronaphthalenes in sulphuric acid.*

Nitro-compound	Nitration (N1) * temp.	HNO_3 (mole)	Yield (%)	Product comp.*	Analysis *
1,2	35°	2	89	1,2,5- 44; 1,2,8- 56	C,P,S
1,3	25	1·5	89	1,3,8- 74; 1,3,5- 26	C,P
1,4	20	1·5	98	1,4,5-	C,P
1,5	30	1·5	94	1,4,5- 94; 1,3,5- 6	C,P,S
1,6	50	3·0	92	1,3,8-	C,P
1,7	25	1·5	91	1,3,5-; 1,4,6-; 1,3,6,8-	C,M
1,8 [a]	75	3·5	60	1,3,8-	
2,3 [b]	50	1·5	88	1,6,7-	
2,6	20	1·5	97	1,3,7-	C,P
2,7	30	1·5	91	1,3,6-	S

* For notes see Table 4.
[a] Hodgson, Ward, and Whitehurst, *J.*, 1945, 450. [b] Coulson, Thesis, London, 1955; Ward, Coulson, and Wells, *J.*, 1957, 4816.

nitronaphthalene). The preponderance of 1-bromo-5-nitronaphthalene was confirmed by paper chromatography and ultraviolet spectroscopy. For 2-nitronaphthalene the product composition by infrared spectroscopic analysis was 1-bromo-7-nitronaphthalene,

[6] Wells and Ward, *Chem. and Ind.*, 1958, 1172.
[7] Derbyshire and Waters, *J.*, 1950, 564, 573.

XUM

TABLE 2. *Nitration of some dinitronaphthalenes in aqueous nitric acid.*

Nitro-compound	Nitration (B1) * time (hr.)	Yield (%)	Product comp.*	Analysis *
1,2	3	57	1,2,5- 70; 1,2,8- 30	C,P
1,3	3	53	1,3,8- 58; 1,3,5- 29; 1,3,5,7- 13	P,M
1,4	3	76	1,4,5- 88; 1,4,6- 12	S,P
1,5	20	52	1,4,5- 34; 1,3,5- 47; 1,3,5,7- 19	P,M
1,6	3	60	1,3,6-; 1,3,8 †	P
1,8	3	66	1,3,8-	P
2,6	6	22	1,3,7-	C,P
2,7	3	—	Unchanged	P

* See Table 4 for notes. † Mainly 1,3,8-.

TABLE 3. *Dinitration of dinitronaphthalenes in sulphuric acid.*

Nitro-compound	Nitration (N1) * temp.	HNO_3 (mole)	Yield (%)	Product comp.*	Analysis *
1,2	80°	14		1,2,5,8-	P,S
1,3	80	17	50	1,3,6,8-	P
1,4	80	14	36	1,3,5,8- 50; 1,4,5,8- 50	P
1,5	80	14	51	1,3,5,8- 50; 1,4,5,8- 50	P
1,6	80	14	60	1,3,6,8-	
1,7	50	4	85	1,3,5,8-	
1,8	80	25	45	1,3,6,8-	
2,3 [a]	70	25	30	1,4,6,7-	
2,6 [b]	80	25	53	1,3,5,7- 81; 1,2,6,8- 16; (?)1,2,4,6- 3	SL
2,7 [b]	75	26	60	1,3,6,8-	

* For notes see Table 4.
[a] Coulson (see Table 1). [b] Chatt and Wynne, *J.*, 1943, 33.

TABLE 4. *Mononitration of some trinitronaphthalenes.*

Nitro-compound	Nitration conditions	HNO_3 (mole)	Yield (%)	Product comp.	Analysis
1,2,8	N1, 80°	9		1,2,5,8-	S
1,3,5	N1, 80°	25	60	1,3,5,8-	S
1,3,5	B1, 20 hr.		42	1,3,5,7-	P
1,3,7	N1, 80°	9		1,3,5,7-; 1,2,6,8-	SL, S
1,4,5	N1, 80°	14	37	1,3,5,8- 33; 1,4,5,8- 67	SL
1,4,5	B1, 12 hr.		51	1,3,5,8-	
1,4,6 [a]	N1, 80°	15	60	1,3,5,8-	

[a] Hardy and Ward, *J.*, 1957, 2634.

Notes on Tables 1—4. The initial compound and nitration products are described by the position of the nitro-groups.

Nitration conditions. N1, sulphuric acid (*d* 1·84)–nitric acid (*d* 1·5). B1, 70% w/w aqueous nitric acid (reflux, excess).

Yield. This represents the yield of polynitronaphthalenes isolated from the nitration product in relation to the original reactant and degree of nitration achieved. The product composition is based on the isolated polynitronaphthalenes.

C, Column chromatography. P, Paper chromatography. S, Infrared spectroscopy. M, Molecular complex formation. SL, Solvent separation.

40 ± 10%; 1-bromo-6-nitronaphthalene, *ca.* 10%; 2-nitronaphthalene, 25 ± 10%; 1,4-dibromo-6-nitronaphthalene, 25 ± 10%, supported by paper and column chromatography.

Since 5-substitution predominates in the case of 1-nitronaphthalene it appears that, possibly owing to its greater size, the brominium ion does not function here in a manner analogously to the nitronium ion. The extensive dibromination of 2-nitronaphthalene and the approximate nature of the analysis prevent us from drawing worthwhile conclusions for this compound.

Three new trinitro- and two new tetranitro-naphthalenes were prepared in these investigations. The mononitration product of 2,6-dinitronaphthalene must be 1,3,7-trinitronaphthalene, since by further nitration it affords 1,3,5,7-tetranitronaphthalene. The higher-melting trinitronaphthalene obtained from 1,2-dinitronaphthalene had a

XUM

dipole moment [8] of 3·65 D in benzene, showing it to be the 1,2,5-isomer. The lower-melting isomer was shown to be the 1,2,8-compound. On further nitration it gave the same product as the 1,2,5-isomer, showing the new tetranitronaphthalene to be the 1,2,5,8-isomer (which differs anyway from the known 1,2,6,8-isomer). The dipole moment of 1,2,8-trinitronaphthalene was 8·84 D. Although this dipole moment is well below the calculated value of 10·8 D (based on 4·0 D for a 1-nitro-group and 4·4 D for a 2-nitro-group [8]) it appears to exclude the 1,2,7-isomer, whose dipole moment would almost certainly be below 8·4 D.

Treating the tetranitronaphthalene from 1,6,7-trinitronaphthalene with sodium *p*-nitrothiophenoxide caused two nitro-groups to be displaced by nucleophilic attack. Since it has been established [9] that in such reactions only nitro-groups in 1,2-, 1,4-, or 2,3-positions in any nucleus are attacked, the 1,3,6,7-isomer is excluded, since this would have only one mobile group. Hence the tetranitronaphthalene is considered to be the 1,4,6,7-isomer, the alternative 1,2,6,7-compound being unlikely since *ortho*-nitration to an α-nitro-group has not been previously observed in the naphthalene series.

Experimental

Analytical Methods.—The procedures for column and paper chromatography were as previously described,[2] except that the alumina used was steeped in 2N-hydrochloric acid for 1 hr. with stirring, washed repeatedly with distilled water, and dried at 120—140° for 18 hr. Trinitronaphthalenes did not decompose on this neutral alumina, the columns usually showing no colour. Tetranitronaphthalenes, however, still suffered considerable decomposition with the production of highly coloured materials. The infrared spectral measurements were made and interpreted by Dr. D. H. Whiffen and Dr. K. Morgan (University of Birmingham).

Nitration Methods.—(a) *Mono- and di-nitration of dinitronaphthalenes* (*or mononitration of trinitronaphthalenes*) *in sulphuric acid* (N1). For mononitration the dinitronaphthalene (1·00 g.) was dissolved in warm sulphuric acid (*d* 1·84; 5 ml.) and then cooled, with stirring, to room temperature to obtain a finely divided suspension. A crystal of sodium nitrite was added and nitric acid (*d* 1·5) run in dropwise with vigorous stirring, the temperature being allowed to rise to, but not exceed, that indicated in Table 1. After 6 hours' stirring and a further 12 hours' storage the polynitronaphthalenes were precipitated by pouring the mixture on ice, collected, repeatedly washed with water, dilute aqueous sodium hydrogen carbonate, and again water, and dried in a vacuum at 60—90°.

For dinitration of dinitronaphthalenes or mononitration of trinitronaphthalenes a similar procedure was followed but during addition of nitric acid the temperature was allowed to rise to 50° and then raised, with vigorous stirring, to 75—90° for 1 hr., the mixture being cooled if frothing became excessive. The product was obtained by pouring the mixture on ice, or the reaction mixture was cooled to −5°; the whole was filtered through sintered glass, the solids were washed with decreasing strengths of aqueous sulphuric acid and finally with water (the filtrates from this were then poured on ice, and precipitates were washed as before).

(b) *Nitration in aqueous nitric acid* (B1). The dinitronaphthalene (1·00 g.) was refluxed with "AnalaR" nitric acid (*d* 1·42; 5 ml.) for 3 hr. and the product isolated by pouring the whole on ice, etc., as above. During refluxing copious brown fumes were evolved and the solution became dark brown.

Individual Nitrations.—These are only described where new compounds were formed or where unusual behaviour occurred which could not be indicated in the Tables.

(a) 1,2-*Dinitronaphthalene*. The product (0·433 g.) was chromatographed in benzene, fractions of 20 ml. being collected. The first five fractions contained 1,2,5-*trinitronaphthalene* (0·169 g.), m. p. 172°, [from ethanol–acetone (1 : 1) m. p. 178° (Found: C, 45·3; H, 1·4; N, 15·8. $C_{10}H_5N_3O_6$ requires C, 45·6; H, 1·9; N, 15·9%). Elution was continued with benzene–ethyl acetate (4 : 1) and the next seven fractions contained 1,2,8-*trinitronaphthalene* (0·214 g.), m. p. 168° (from benzene) (Found: C, 45·7; H, 1·9%). Coloured bands remained at the top of the column. Quantities up to 5 g. of product were separated in this manner.

[8] Richards, Sharpe, and Walker, unpublished work.
[9] Coulson, Thesis, London, 1955; Hodgson and Ward, *J.*, 1948, 2017; Ward and Day, *J.*, 1952, 4529.

XUM

The dipole moments of these compounds were measured (by Dr. S. Walker and Mr. A. N. Sharpe) in benzene solution at 25° ± 0·01°, by the method described by Cumper, Vogel, and Walker [10] and calculated by the method of Halverstadt and Kumler.[11] The dielectric constants were obtained by using a heterodyne capacitance meter based on a circuit described by Weissberger,[12] but incorporating a cathode-ray oscilloscope to detect the balance point.

1,2,5,8-*Tetranitronaphthalene* had m. p. 190—192° (Found: C, 39·7; H, 1·0; N, 17·5. $C_{10}H_4N_4O_8$ requires C, 39·0; H, 1·3; N, 18·2%).

(b) 1,3-*Dinitronaphthalene*. The reaction product from aqueous nitric acid (3·34 g.) was crystallised from benzene, giving pure 1,3,8-trinitronaphthalene (1·410 g.). The filtrate was treated with 2-naphthol (1·2 g.) in benzene (5 ml.), and the orange precipitate collected. Fractional crystallisation of this from chloroform gave first the red complex (0·49 g.) of 1,3,5,7-tetranitronaphthalene and then the orange complex (1·09 g.) of 1,3,5-trinitronaphthalene.

(c) 1,7-*Dinitronaphthalene*. A solution of the mononitration (N1) product (1·00 g.) in hot benzene (20 ml.) was treated with one of 2-naphthol (0·80 g.) in benzene (10 ml.). Cooling produced the red complex of 1,3,5-trinitronaphthalene, further crystallised from chloroform (0·51 g., 33% of 1,3,5-trinitronaphthalene in the original nitration product). Chromatography of the benzene filtrate gave 1,4,6-trinitronaphthalene (0·30 g., 30%), and paper chromatography showed this to be free from other polynitronaphthalenes. When the nitration product was chromatographed on alumina in benzene, paper chromatography of the fractionated product showed the presence of 1,3,5- and 1,4,6-trinitronaphthalene, and in the final fraction 1,3,5,8-tetranitronaphthalene.

(d) 2,3-*Dinitronaphthalene* (with T. M. Coulson). 1,4,6,7-*Tetranitronaphthalene* had m. p. 186° (from ethanol) (Found: C, 39·0; H, 1·4; N, 18·2. $C_{10}H_4O_8N_4$ requires C, 39·0; H, 1·3; N, 18·2%). It was dissolved in ethanol (12 ml.) and refluxed with *p*-nitrothiophenoxide (0·18 g.) in ethanol (2 ml.) containing sodium hydroxide (0·06 g.), for 30 min., the whole was cooled and poured on ice, and the solid collected. Chromatography on acid-washed alumina in benzene gave an almost quantitative yield of a *dinitrodi-*(p-*nitrophenylthio*)*naphthalene*, m. p. 126° (Found: C, 51·2; H, 2·98; N, 10·5; S, 11·7. $C_{22}H_{12}N_4O_8S_2$ requires C, 50·4; H, 2·29; N, 10·7; S, 12·2%).

(e) 2,6-*Dinitronaphthalene*. 1,3,7-*Trinitronaphthalene* had m. p. 155° (from alcohol–acetone, 1 : 1) (Found: C, 46·2; H, 2·0; N, 16·2%). With 2-naphthol in benzene, it gave a red complex (from chloroform), m. p. 120°. 1,3,5,7-Tetranitronaphthalene was separated from the nitration product of 1,3,7-trinitronaphthalene, and 1,2,6,8-tetranitronaphthalene (but not the 1,2,4,6-isomer [13]) detected in this by infrared spectroscopy.

Competitive Nitration of 1- *and* 2-*Nitronaphthalene*.—A solution of 1-nitronaphthalene (1·030 g.) and 2-nitronaphthalene (0·441 g.) in sulphuric acid (*d* 1·84; 12 ml.) was treated dropwise, with vigorous stirring, at 0° with a 4 : 1 v/v mixture of sulphuric acid (*d* 1·84) and nitric acid (*d* 1·42), 0·60 ml. being used, which was sufficient for *ca.* 25% of mononitration. The mixture was then poured on ice, the whole extracted with ether (3 × 75 ml.), the extract dried (Na_2SO_4, 5 g.; $NaHCO_3$, 5 g.) overnight, filtered through alumina, and evaporated (residue 1·573 g., 27% mononitration). This (0·392 g.) was chromatographed in benzene (20 ml.) on alumina (55 × 2 cm.) made up in 1 : 1 v/v benzene–light petroleum (b. p. 40—60°), and the yellow band of mixed mononitronaphthalenes eluted with this solvent (yield 0·260 g., 28·7% mononitration). Ultraviolet spectroscopy [14] showed the presence of 71% of 1- and 29% of 2-isomer. Hence 1·041 g. of unchanged mononitronaphthalenes contained 0·741 g. of 1- and 0·300 g. of 2-isomer. Hence the relative reactivities are 1-nitronaphthalene : 2-nitronaphthalene = 0·9 : 1. Repetition of the experiment gave a ratio 1·0. (The calculations were carried out as by Dewar *et al.*[15])

1- (0·728 g.) and 2-Nitronaphthalene (0·597 g.) in acetic anhydride (10 ml.) were nitrated, dropwise with vigorous stirring, at 0° with nitric acid (*d* 1·5; 0·10 ml.), and the solution then slowly raised to 60° and afterwards kept for 1 hr. The mixture was poured into water (500 ml.) containing sulphuric acid (*d* 1·84; 1 ml.), kept overnight, and extracted with chloroform (250 ml.). The extract was repeatedly washed with water, dried, filtered, and evaporated

[10] Cumper, Vogel, and Walker, *J.*, 1956, 3621.
[11] Halverstadt and Kumler, *J. Amer. Chem. Soc.*, 1942, **64**, 2988.
[12] Weissberger, "Physical Methods of Organic Chemistry," Vol. I, Interscience Publ. Inc., New York, 1938.
[13] Chatt and Wynne, *J.*, 1943, 33.
[14] Dewar and Urch, *J.*, 1957, 345.
[15] Dewar, Mole, and Warford, *J.*, 1956, 3576.

XUM

(residue 1·355 g., 8·6% mononitration). Chromatography, as above, indicated that 8·3% of mononitration had occurred, the composition of the mixed mononitronaphthalenes being 1-54·8% and 2-isomer, 45·2%, giving the relative reactivities as 1·1 : 1.

The authenticity of these experiments was verified as follows. Appropriate amounts of pure 1- and 2-nitronaphthalene, 1,5-, 1,6-, 1,7-, and 1,8-dinitronaphthalene were chromatographed in benzene on alumina. Separation of the mono- from the di-nitronaphthalenes was excellent. Infrared spectroscopy of the recovered mononitro-compounds showed the absence of dinitronaphthalenes and the composition was in reasonable agreement with that expected (Found: C, 69·7; H, 4·2; N, 7·8. Calc. for $C_{10}H_7NO_2$: C, 69·5; H, 4·05; N, 8·1%).

Bromination of 1- *and* 2-*Nitronaphthalene.*—1-Nitronaphthalene (2·0 g., 0·011 mole) and powdered silver sulphate (2·0 g.) in sulphuric acid (*d* 1·84; 10·4 ml.) and water (1·2 ml.) were treated with bromine (0·60 ml.; 0·011 mole) at −5° and shaken at room temperature for 3 hr., then poured on ice. The solids were collected, dried, and extracted with benzene. The extract was passed through a short alumina column; evaporation then gave a yellow oil which slowly solidified (2·46 g.) but was not separable by column chromatography. 2-Nitronaphthalene gave similar results but in this case pure 1,4-dibromo-6-nitronaphthalene was separated by column chromatography in benzene on alumina.

Discussion

Since the results given in Parts II and III of this series are based on improved nitration techniques and analytical methods this discussion largely ignores our earlier theoretical interpretations of the nitration of the polynitronaphthalenes.[1,16] The factors to be considered, in order of importance, are as follows.

(a) *The naphthalene polarisability.* This favours α- over β-substitution for all types of reaction (electrophilic, nucleophilic, and free-radical), as was implicit in the theories of Armstrong and Wynne,[17] Veselý and Jakeš,[18] and Hodgson *et al.*,[16] and has now received theoretical support from Dewar.[19]

(b) *The electronic effects of the nitro-group on the nucleus and their modification by the reagent.* For the nitro-group, inductive effects predominate (*i.e.*, I_σ, I_π, and direct field effects); the mesomeric effect is much smaller, and the *E*-effect negligible for electrophilic substitution.[20]

(c) *Steric effects.* If the deactivating influence of the nitro-group is exerted mainly through its inductive effect, rotation of the group out of the plane of the ring by steric interaction with a *peri*-hydrogen atom of a further nitro-substituent will not greatly diminish the magnitude of this influence or its effect on further nitration. The situation is complicated by the possible intervention of the *D*-effect.[2,6]

(d) *Miscellaneous factors.* We shall not discuss here factors such as temperature, modification of substrate and reagent by solvation, etc., except to point out the possible intervention of the nitric acidium ion in aqueous nitric acid nitrations already referred to.[2]

Attempts to make a comprehensive assay of the results in terms of classical electronic theory provided only a limited interpretation. Application of molecular-orbital theory, however, gave a much more satisfactory overall interpretation of both the qualitative and the quantitative results.

Dewar and Maitlis, using modified molecular-orbital theory, accounted satisfactorily for the nitration of quinoline, isoquinoline, cinnoline, quinoxaline, and quinazoline in sulphuric acid. The results parallel those for the further nitration of the mono- and di-nitronaphthalenes if we assume that the hetero-atom is replaced by the carbon atom

[16] Hodgson and Ward, *J. Soc. Dyers and Colourists*, 1947, **63**, 141, 177.
[17] Armstrong and Wynne, *J.*, 1877, **31**, 258.
[18] Veselý and Jakeš, *Bull. Soc. chim.*, 1923, **33**, 925.
[19] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341, 3345, 3350, 3353, 3355, 3357.
[20] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, 252; Wepster, "Progress in Stereochemistry," Butterworths, London, 1958, Vol. II; Jaffé, *Chem. Rev.*, 1953, **53**, 191; Roberts and Moreland, *J. Amer. Chem. Soc.*, 1953, **75**, 2167.

XUM

bearing the nitro-substituent. In any case, the equation [19] for the effect of a $+E$ substituent (Dewar's nomenclature) is too complicated for practical use; therefore, the effect of a substituent of this kind on the stability of the transition state may be taken as approximately Ca^2, where C is made equal to α, the " coulomb term " of the composite nitro-group and carbon to which it is attached.

Hence, the equation

$$\Delta E_\pi' = \Delta E_\pi + \Sigma \alpha_r a_{or}^2$$

may be applied (Dewar's paper [21] should be consulted for the terminology and method of application of this equation).

This treatment would be completely valid if the NMBO coefficients of the hetero-atom were zero, which would be the case if the C–N bond were entirely single. This is, of course, an approximation, but, as already pointed out, the nitro-group (and indeed all electronegative substituents) appear to have large inductive and only small mesomeric effects, the latter also being of diminished importance in the stabilisation of the transition state of an electrophilic substitution.

The results of the calculations by Dewar and Maitlis's method are tabulated here. A value of -4 kcal. mole^{-1} for β^* was assumed by Dewar and Maitlis for nitration in concentrated sulphuric acid and has been used here. A value of -5 kcal. mole^{-1} has been assumed for α, as this gives the best overall agreement with the experiments considered. Table 5 shows the calculated effects of the naphthalene polarisability and the 1- and 2-nitro-group on the naphthalene nucleus in the transition state of naphthalene substitution; Table 6 shows the results calculated for the dinitronaphthalenes when the effects of the nitro-groups are assumed to be additive.

TABLE 5. *Activation energies for nitration of the mononitronaphthalenes.*

Position of further substn. ...	1	2	3	4	5	6	7	8
Naphthalene	7·24	8·48	8·48	7·24	7·24	8·48	8·48	7·24
1-NO_2	—	2·50	0·42	1·82	0·46	0·42	0·63	0·30
1-Nitronaphthalene	—	10·98	8·90	9·06	7·70	8·90	9·11	7·54
2-NO_2	1·82	—	0·63	1·23	0·30	0·63	0·42	0·46
2-Nitronaphthalene	9·06	—	9·11	8·47	7·54	9·11	8·90	7·70

TABLE 6. *Activation energies for nitration of the dinitronaphthalenes.**

$(NO_2)_2C_{10}H_6$	1	2	3	4	5	6	7	8
1,2	—	—	9·5	10·3	**8·0**	9·5	9·5	**8·0**
1,3	—	11·6	—	10·9	*8·2*	9·3	9·7	**7·8**
1,4	—	11·4	11·4	—	**8·0**	9·5	9·5	**8·0**
1,5	—	11·4	*9·5*	**9·4**	—	11·4	*9·5*	**9·4**
1,6	—	11·6	9·3	9·5	9·5	—	9·7	**8·8**
1,7	—	11·4	9·5	**9·4**	**8·9**	9·5	—	9·4
1,8	—	11·6	**9·3**	9·5	9·5	**9·3**	11·6	—
2,3	10·3	—	—	10·3	**8·0**	9·5	9·5	**8·0**
2,6	9·4	—	9·5	**8·9**	9·4	—	9·5	**8·9**
2,7	9·6	—	9·7	**8·8**	**8·8**	9·7	—	9·5

* The figures for the positions where predominant nitration occurs are in bold types and those where a small amount of nitration occurs in italics.

The agreement with experiment is good. The figures are essentially the same as those of Sixma. The method of calculation in both cases is based on molecular-orbital theory, but Sixma assumes that the influence of the inductive effect of the nitro-group is due to the electrostatic field of the substituent (the direct field effect). As well as forecasting correctly the positions of further substitution, these results give the order of reactivity of the individual polynitronaphthalenes as follows (the trinitronaphthalenes being taken from Sixma's calculations):

$$1 = 2 > 1,3 > 1,4 = 1,2 = 2,3 > 1,6 = 2,7 > 1,7 =$$
$$2,6 > 1,8 > 1,5 > 1,3,6 > 1,4,6 > 1,3,7 > 1,3,8 > 1,3,5 > 1,4,5 > 1,2,5 > 1,2,8 > 1,6,7.$$

[21] Dewar and Maitlis, *J.*, 1957, 2521.

This order is in agreement with the preliminary experiments carried out. Moreover, the three most reactive trinitronaphthalenes are those given by the three dinitronaphthalenes (1,7-, 2,6-, and 2,7-) which appear to be most easily nitrated. However, it should be noted that no satisfactory reason can be given for the anomalous case of 2-nitronaphthalene, where mononitration yields a proportion of 5- to 8-substitution opposite to that expected on theoretical grounds.

The authors thank Mr. J. G. Hawkins, B.Sc., for some preliminary experiments, and the National Smelting Company (Avonmouth) for gifts of chemicals.

LEICESTER COLLEGE OF TECHNOLOGY AND COMMERCE,
LEICESTER.

[*Received, September 22nd,* 1960.]

---

852. *The Existence of the* P¹P¹-*Diethyl Pyrophosphate Ion.*

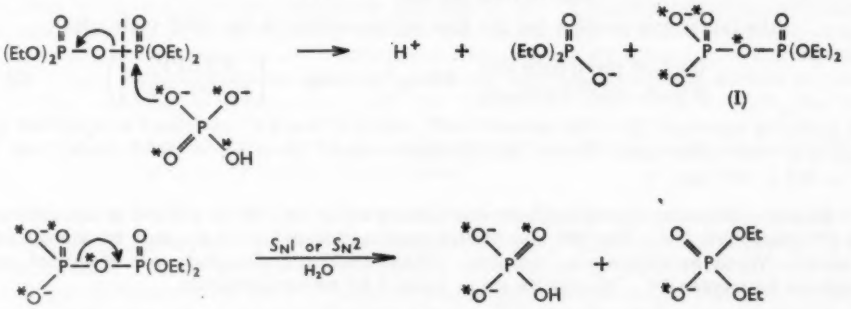
By DAVID SAMUEL and B. SILVER.

The phosphate-catalysed hydrolysis of tetraethyl pyrophosphate has been studied with the aid of oxygen-18. It is shown to proceed *via* the *P*¹*P*¹-diethyl pyrophosphate ion, whose existence had been suggested previously on the basis of kinetic results.

THE *P*¹*P*¹-dialkyl pyrophosphate ion has been postulated as an intermediate in the hydrolysis of tetramethyl [1] and tetraethyl pyrophosphate,[2] catalysed by phosphate ions, in the pH range 7·9—9·2. An analogous ion has been suggested as intermediate in the synthesis of nucleotides when tetra-*p*-nitrophenyl phosphate is used as phosphorylating agent.[3] The only products of the hydrolyses are the corresponding dialkyl phosphate and phosphate ion. The mechanism proposed [2] involves nucleophilic (S_N2) attack by the phosphate ion on a phosphorus atom of the pyrophosphate to form the hypothetical *P*¹*P*¹-dialkyl phosphate ion, subsequent hydrolysis of which could proceed by either an S_N1 or an S_N2 mechanism.

The *P*¹*P*¹-dialkylpyrophosphate ion (I; not labelled) was not isolated, its formation being inferred mainly from kinetic evidence.[1,2] When Avison [2] suggested that this reaction may serve as a model for phosphate transfer in biological systems, the possibility of an ion (I) acquired additional interest. The present work describes the use of oxygen-18 as a tracer which confirms its existence.

The hydrolysis of tetraethyl pyrosphate in the presence of [^{18}O]phosphate ion is represented in the annexed scheme. By the catalytic path each molecule of tetraethyl



pyrophosphate (TEPP) produces 2 molecules of diethyl phosphate (DEP) containing a total of 8 oxygen atoms, one of which will be enriched: the simultaneous non-catalysed

[1] Brown and Hamer, *J.*, 1960, 1155.
[2] Avison, *J.*, 1955, 732.
[3] Hampton and Maguire, *J. Amer. Chem. Soc.*, 1961, **83**, 150.

XUM

hydrolysis produces phosphate that is not enriched. The percentage enrichment of diethyl phosphate therefore depends on the relative rates of the catalysed and the non-catalysed reaction:

$$\text{Catalysed: } d[DEP]_t/dt = k[P][TEPP]_t = -d[TEPP]_t/dt. \quad (1)$$

$$\text{Not catalysed: } d[DEP]_t/dt = k'[TEPP]_t = -d[TEPP]_t/dt. \quad (2)$$

From (1) and (2) we have

$$[TEPP]_t = [TEPP]_0 \exp\{-(k[P] + k')t\},$$

where $[P] = [HPO_4^{2-}]$.

The final enrichment of diethyl phosphate may be calculated as follows: We define

$$\alpha_t = \frac{\text{Total excess moles } {}^{18}O \text{ in phosphate ion}}{\text{Total number of moles of phosphate ion}} \text{ at time } t.$$

Then, the number of moles of ^{18}O lost per second from phosphate ion at time t is

$$-[P]\frac{d\alpha_t}{dt} = -\frac{\alpha_t}{4} \cdot \frac{d[TEPP]_t}{dt} \text{ (catalysed)} = -\frac{\alpha_t}{4} k[P][TEPP]_t$$

$$= -\frac{\alpha_t}{4} k[P][TEPP]_0 \exp\{-(k[P] + k')t\}.$$

Rearranging and integrating this expression gives

$$\int_0 \frac{d\alpha_t}{dt} = \frac{k}{4} \cdot [TEPP]_0 \int_0^\infty \exp\{-(k[P] + k')t\} \cdot dt$$

Then

$$\ln \frac{\alpha_0}{\alpha_\infty} = \frac{k}{4} \cdot \frac{[TEPP]_t}{k[P] + k'}.$$

I.e.,

$$\alpha_0/\alpha_\infty = \exp\left[\frac{k[TEPP]_0}{4(k[P] + k')}\right].$$

The total loss of oxygen-18 from phosphate ion after complete hydrolysis of the pyrophosphate is $(\alpha_0 - \alpha_\infty)$ (mol. of phosphate ion). This is also the number of mols. of diethyl phosphate each containing one atom of oxygen-18; so the excess percentage enrichment of the diethyl phosphate after complete hydrolysis is:

$$\frac{(\text{mol. of phosphate ion})\ (\alpha_0 - \alpha_\infty)}{\text{mol. of DEP formed}} \times \tfrac{1}{4} \times 100$$

(the factor $\frac{1}{4}$ is to allow for the four oxygen atoms in the DEP molecule)

$$= \frac{(\text{mol. of phosphate ion})}{4\ (\text{mol. of DEP formed})} \cdot 100\alpha_0 \left(1 - \exp - \left[\frac{k[TEPP]}{4(k[P] + k')}\right]\right). \quad (3)$$

In applying equation (3) to the present work, values of k and k', as defined in equations (1) and (2), were taken from Brown and Hamer's work[1] ($k = 8{\cdot}8 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$; $k' = 3{\cdot}3 \times 10^{-4}$ sec.$^{-1}$).

Results.—Tetraethyl pyrophosphate was hydrolyzed at 58—60° at pH 8·8 in the presence of [^{18}O]phosphate ion. The pH and temperature correspond to those used by Brown and Hamer.[1] When hydrolysis was complete, diethyl hydrogen phosphate was recovered and analysed for oxygen-18. The results are in Table 1 for two experiments.

TABLE 1. *Hydrolysis of tetraethyl pyrophosphate in the presence of* [^{18}O]*phosphate ion, at* pH 8·8 *and* 59° ± 1°.

[TEPP] (mole l.$^{-1}$)	[P] (mole l.$^{-1}$)	Initial excess atom % ^{18}O in phosphate ion	Excess atom % ^{18}O in DEP	Excess atom % ^{18}O in DEP, calc. from eqn. (3)
0·033	0·1	12·1	0·915, 0·908	1·05

XUM

Inorganic phosphate was recovered quantitatively by precipitation as barium phosphate and was analysed for oxygen-18. The total amounts of oxygen-18 in the products are shown in Table 2.

TABLE 2.

^{18}O in DEP (μ mole)	^{18}O in phosphate after reaction (μ mole)	O^{18} recovered (μ mole)	Initial O^{18} in phosphate (μ mole)	Recovery of ^{18}O (%)
146·4	2832	2978	2904	102·6
145·3	2829	2974	2904	102·4

It is necessary to consider alternative paths whereby oxygen-18 could be incorporated into diethyl phosphate. Preliminary exchange between phosphate ion and the solvent water and subsequent exchange between enriched water and diethyl phosphate may be excluded on two grounds. Oxygen-18 exchange between phosphate ion and water at pH 9 is virtually undetectable under the experimental conditions,[4] and even if exchange had been complete the final excess percentage enrichment of the water would be less than 0·1%. Subsequent exchange between water and diethyl phosphate could not account for the observed enrichment of 0·91% in diethyl phosphate. Another path for oxygen-18 transfer to diethyl phosphate might be an exchange between labelled phosphate ion and diethyl phosphate; two solutions, each containing diethyl hydrogen phosphate (0·1M) and disodium hydrogen phosphate (0·4M) (12·1 excess atom % of ^{18}O), were adjusted to pH 8·8 by sodium hydroxide and kept at 60° for 2 and 4 hr. severally; the recovered diethyl hydrogen phosphate contained 0·004 and 0·000 excess atom % of ^{18}O, which excludes this mode of exchange.

Experimental.—The hydrolyses were carried out, with stirring, in a beaker kept at 59° ± 1°. Tetraethyl pyrophosphate (2 μmoles) was added rapidly to a solution of disodium hydrogen phosphate (6 μmoles) (12·1 excess atom % of O^{18}) in water (60 ml.). Carbon dioxide-free N-sodium hydroxide was run in at a rate sufficient to maintain the pH at 8·7—8·9 (as measured by a glass electrode). Isolation of the products was begun after 90 min. (~9 half-lives). The isolation procedures given below were also used in obtaining the results of the exchange experiments mentioned in the preceding paragraph.

Isolation of inorganic phosphate. Inorganic phosphate was precipitated with a slight excess of barium hydroxide solution. The precipitate was filtered off, washed in water, and dissolved in N-hydrochloric acid, and the solution was filtered. Barium phosphate was reprecipitated by the addition of sodium hydroxide solution, and the precipitate centrifuged off and washed with water before being dried in a vacuum oven.

Isolation of diethyl hydrogen phosphate. The filtrate from the first barium phosphate precipitate was treated as follows: To ensure complete removal of [^{18}O]phosphate ion, an isotopic dilution was carried out. The pH of the solution was adjusted to 2—3 with N-hydrochloric acid, and disodium hydrogen phosphate (2·5 μmoles) and barium chloride (3·8 μmoles) were dissolved in it. The pH was adjusted to 8—9 with aqueous sodium hydroxide, and the resulting precipitate of barium phosphate was filtered off. A solution of barium hydroxide (2 μmoles) was added to the filtrate which was then concentrated to a final volume of ~3 ml. in a vacuum at room temperature. Addition of 4 volumes of 95% ethanol gave a precipitate of the barium diethyl phosphate, which was centrifuged off, washed with 80% ethanol, acetone, and ether, and dried in a vacuum at about 70° (Found: P, 13·8. Calc. for $C_4H_{10}Ba_{\frac{1}{2}}O_4P$: P, 14·0%).

Oxygen-18 analyses of the barium phosphate and barium diethyl phosphate were carried out by the method given by Anbar and Guttmann.[5]

Discussion.—The results show that the hydrolysis of tetraethyl pyrophosphate in the presence of [^{18}O]phosphate ion produces diethyl hydrogen [^{18}O]phosphate. The percentage enrichment of this agrees reasonably with that expected on the basis of a catalysed path involving the formation of the P^1P^1-diethyl pyrophosphate ion as an intermediate. Alternative paths for oxygen-18 transfer have been excluded by showing the absence of oxygen-18 exchange between diethyl hydrogen phosphate and phosphate ion under the experimental conditions obtaining during the hydrolysis.

[4] Silver, unpublished results.
[5] Anbar and Guttmann, *J. Appl. Rad. Isotopes*, 1958, **3**, 131.

XUM

In conjunction with the mainly kinetic results of previous studies, this work strongly supports the existence of the P^1P^1-diethyl pyrophosphate ion.

This investigation was supported in part by a grant from the Division of Research Grants, U.S. Public Health Service. One of us (B. S.) is the holder of a Max and Rebecca Schrire Medical Research Grant.

WEIZMANN INSTITUTE OF SCIENCE,
REHOVOTH, ISRAEL.

[*Received, March* 21*st*, 1961.]

---

853. *The Rôle of Peroxides in the Autoxidation of Elaidic Acid and Oleic Esters.*

By GEORGE KING.

The effect of heat on autoxidised elaidic acid, and methyl and ethyl oleates, has been studied in order to elucidate the secondary changes resulting from the decomposition of hydroperoxides. Fractions enriched in peroxides have been prepared by the urea method.[1,2]

The decomposition of the peroxides at 80—90° appears to give rise invariably to hydroxy-compounds and, in the early stages of autoxidation, αβ-unsaturated ketones, but not to epoxides. Thermal decomposition of peroxide-enriched fractions from oleic esters yields also other carbonyl compounds, in which the carbonyl group is not vicinal to the double bond. Autoxidised elaidic acid similarly gives significant amounts of ketols and of unsaturated compounds of undetermined constitution, which may be oxygen-bonded but contain no other functional group. Chain scission at the double bond during this process is inextensive.

The epoxide in autoxidised methyl oleate has been established by isolation of the epoxy-acid as mainly, if not entirely, the *trans*-form.

CONSIDERABLE importance is attached to the rôle of peroxides in the autoxidation of olefins. The active peroxides which are formed at an early stage in the autoxidation of oleic and elaidic acids and their alkyl esters appear to be mainly hydroperoxides of the type R·CH(O·OH)·CH:CH·R′, in which the double bond remains intact, although perhaps partly displaced from its original position.[3,4,5] These are commonly thought to give rise by thermal decomposition, or reaction with unchanged olefin, to 8- and 11-oxo-derivatives [(I) and (II) respectively] and epoxides:[6,2,5,7]

(I) $CH_3\cdot[CH_2]_7\cdot CH{:}CH\cdot CO\cdot[CH_2]_6\cdot CO_2R$ $\quad$ $CH_3\cdot[CH_2]_6\cdot CO\cdot CH{:}CH\cdot[CH_2]_7\cdot CO_2R$ (II)

The rearrangement of hydroperoxides to ketols has also been postulated.[8] However, much uncertainty remains concerning the sequence of changes and mechanisms involved in the autoxidation process,[9,10] and further work in this field was felt to be desirable.

Although substantially pure hydroperoxide fractions have been prepared from

[1] Coleman, Knight, and Swern, *J. Amer. Chem. Soc.*, 1952, **74**, 4886.
[2] Coleman, Knight, and Swern, *J. Amer. Oil Chemists' Soc.*, 1955, **32**, 135.
[3] Waters, *Ann. Reports*, 1945, **42**, 130.
[4] Swern, Coleman, Knight, Ricciuti, Willits, and Eddy, *J. Amer. Chem. Soc.*, 1953, **75**, 3135.
[5] Swern and Coleman, *J. Amer. Oil Chemists' Soc.*, 1955, **32**, 700.
[6] Farmer, Bloomfield, Sundralingam, and Sutton, *Trans. Faraday Soc.*, 1942, **38**, 348; Swift and Dollear, *J. Amer. Oil Chemists' Soc.*, 1948, **25**, 52.
[7] King, *J.*, 1954, 2114; 1956, 587.
[8] Skellon, *J.*, 1948, 343; Swern, Scanlan, and Knight, *J. Amer. Oil Chemists' Soc.*, 1948, **25**, 193.
[9] Cf. Szent-Györgyi, *Biochem. Z.*, 1924, **146**, 246; Farmer and Sundralingam, *J.*, 1942, 121.
[10] Ellis, *Biochem. J.*, 1950, **46**, 129.

XUM

autoxidised methyl oleate,[11,2,12] relatively little is known about their subsequent decomposition. Thermal decomposition of these hydroperoxides gives rise at 100° to hydroxy-compounds,[12] at 150—260° to αβ-unsaturated carbonyl compounds, including 2-undecenal,[13] and at 210° to dimeric products.[14] Swift and Dollear [6] failed to isolate either epoxy- or dihydroxy-compounds when the hydroperoxides were heated alone under nitrogen, but when heated with oleic acid at 90° small yields of *threo*-9,10-dihydroxystearic acid and oleic acid epoxide were isolated from the acidic fraction. O'Neill [15] heated methyl oleate hydroperoxide with methyl oleate and obtained mainly oxygen-bonded products.

Preliminary observations on the effect of heat on autoxidised elaidic acid have already been reported.[16] The urea-complex method,[1,2] by which most of the epoxides and unchanged acid (or ester) are removed as inclusion compounds, has now afforded a convenient means of preparing suitable fractions containing 25—40% or more of peroxides from elaidic acid or oleic esters, following mild autoxidation at 50° or 82—83°. When these fractions are heated without a catalyst at about 85° under nitrogen for 2 days, the active peroxides are largely destroyed, and a marked rise in the total carbonyl and αβ-unsaturated-

TABLE 1.

Effect of heat on the products obtained by autoxidising elaidic acid at 50° for 23 days: (A) whole product; (B) fraction not forming urea complex; (C) fraction forming urea complex. (i) Before, (ii) after being heated under N_2 at 85° for 24 hr.

	(A)		(B)		(C)	
	(i)	(ii)	(i)	(ii)	(i)	(ii)
Physical condition	Mainly crystalline	Slightly yellow, oily crystals	Oil	Pale yellow, thick oil	Slightly oily crystals	Slightly yellow, semi-solid
Reduction of Fehling's soln.	Slight	Slight	Slight	Slight	None	Trace
Equivalent weight	300	320	342	324	299	317
Iodine value	61	62	56	57	67	68
$E^{1\%}_{1\,cm.}$ at 224 mμ	36·7	40·3	32·0	56·9	38·3	33·5
Neutral, steam-volatile oil (mainly nonanal and nonan-2-one) (%)	2·51	1·18	5·15	2·67	0·31	0·24
Volatile oil (nonanal and nonanone) resulting from hydrolysis on distn. with 0·5N-NaOH (%)	3·09	3·08	3·46	4·50	3·42	2·92
Nonanal on distn. of the residual solution from the above hydrolysis with KIO_4 at pH 8·0 (%)	3·21	5·85	5·18	5·31	1·56	3·64
Saponification value	46	53	88	78	15	23
Nonanal resulting from oxidn. with KIO_4 at pH 8·0 (%)	0·16	1·19	0·51	1·47	0·12	0·26
Carbonyl (%)	1·06	1·52	0·93	2·13	0·81	0·84
Oxiran-O (%)	0·64	0·26	0·01	0·00	1·08	0·77
Active O (%)	0·52	0·01	1·22	0·15	0·06	0·02
OH value (corrected for hydroperoxide and epoxide)	42	55	78	92	0	17
Steam-volatile acids, mequiv. (%)	48	43	62	70	18	33
Non-volatile, water-soluble acids, mequiv. (%)	43	32	51	42	4	3

ketone content occurs (Tables 1—8, columns B). The observed increase in the latter rarely exceeds 25% of that calculated for the simple dehydration $\cdot CH(O\cdot OH)\cdot CH{:}CH\cdot \longrightarrow \cdot CO\cdot CH{:}CH\cdot$, or 50% for the intermolecular oxidation $2\cdot CH(O\cdot OH)\cdot CH{:}CH\cdot + \cdot CH_2\cdot CH{:}CH\cdot \longrightarrow 2\cdot CH(OH)\cdot CH{:}CH\cdot + \cdot CO\cdot CH{:}CH\cdot + H_2O$, but there may be some

[11] Farmer and Sutton, *J.*, 1943, 119; Swift, Dollear, and O'Connor, *Oil and Soap*, 1946, **23**, 355.
[12] Holman, Nickell, and Privett, *J. Amer. Oil Chemists' Soc.*, 1958, **35**, 422.
[13] Swift, Dollear, Brown, and O'Connor, *J. Amer. Oil Chemists' Soc.*, 1948, **25**, 39.
[14] Frankel, Evans, and Cowan, *J. Amer. Oil Chemists' Soc.*, 1960, **37**, 418.
[15] O'Neill, *Chem. and Ind.*, 1954, 384.
[16] King, *J.*, 1958, 1485.

XUM

TABLE 2.

Approximate composition (%), calculated from Table 1, of the products obtained by autoxidising elaidic acid at 50° for 23 days.

	(A)		(B)		(C)	
	(i)	(ii)	(i)	(ii)	(i)	(ii)
8- and 11-Oxoelaidic acids, $C_{18}H_{32}O_3$ deduced from { (a) $E^{1\%}_{1\,cm.}$ at 224 mμ	6·8	7·5	6·0	10·5	7·1	6·2
{ (b) hydrolysis	7·3	7·3	8·3	10·2	8·0	7·0
9,10-Ketol-acids, as $C_{18}H_{34}O_4$	0·9	6·6	2·8	8·2	0·6	1·5
Other oxo-acids, as $C_{18}H_{32}O_3$	0·0	0·0	0·0	0·0	0·2	0·8
9,10-Epoxystearic acid	11·9	4·8	0·3	0·0	20·1	14·4
Hydroperoxyelaidic acids	10·2	0·2	24·0	2·9	1·1	0·3
9,10-Dihydroxystearic acid (combined)	5·6	10·2	11·6	9·7	1·0	6·3
Hydroxyelaidic acids	16·0	13·4	27·9	32·0	0·0	1·9
Other unsaturated products and unchanged elaidic acid, as $C_{18}H_{34}O_2$	36·8	49·3	8·2	20·7	66·6	67·3
Steam-volatile acids, as nonanoic	7·7	6·8	9·9	11·1	2·8	5·3
Non-volatile, water-soluble acids, as azelaic	4·1	3·0	4·8	4·0	0·4	0·3
Neutral, steam-volatile oil	2·5	1·2	5·1	2·7	0·3	0·2

TABLE 3.

Effect of heat on the products obtained by autoxidising elaidic acid at 82° for 24 hr.: (A) whole product; (B) fraction not forming urea complex; (C) fraction forming urea complex. (i) Before, (ii) after being heated under N_2 at 83° for 2 days.

	(A)		(B)		(C)	
	(i)	(ii)	(i)	(ii)	(i)	(ii)
Physical condition	Oily crystals	Slightly yellow oily crystals	Viscous oil	Dark thick oil	Oily crystal-line	Oily crystal-line
Reduction of Fehling's soln.	None	Slight	None	Slight	Trace	Trace
Equiv. wt.	294	318	347	350	289	308
Iodine value	71	69	61	61	74	76
$E^{1\%}_{1\,cm.}$ at 224 mμ	19	22	30	57	12	11
Neutral, steam-volatile oil (mainly nonanal and nonan-2-one) (%)	0·5	0·4	1·2	1·8	0·2	0·3
Volatile oil (nonanal and nonanone) resulting from hydrolysis on distn. with 0·5N-NaOH (%)	1·25	2·0	3·69	4·72	1·05	1·03
Nonanal on distn. of the residual solution from the above hydrolysis with KIO_4 at pH 8·0 (%)	2·09	3·85	3·4	3·8	1·03	4·24
Saponification value	40	56	72	72	16	33
Nonanal resulting from oxidn. with KIO_4 at pH 8·0 (%)	0·00	0·95	0·70	1·50	0·28	0·80
Carbonyl (%)	0·38	0·70	0·40	2·17	0·13	0·48
Oxiran-O (%)	0·56	0·27	0·03	0·00	0·59	0·19
Active O (%)	0·46	0·01	1·31	0·01	0·03	0·002
OH value (corrected for hydroperoxide and epoxide)	41	57	76	101	21	31
Steam-volatile acids, mequiv. (%)	29	25	37	38	10	13
Non-volatile, water-soluble acids, mequiv. (%)	56	41	26	27	1·0	1·3

concurrent decomposition. The former process, which is typical of the catalysed decomposition of cyclic hydroperoxides,[3] should lead to unsaturated ketones in which the *trans*-configuration predominates, since the hydroperoxides themselves, even when derived from oleate, appear to be mainly the *trans*-forms.[17,4,5,12] Ketones of this type are normally isolable without difficulty,[18,16] yet neither (I) nor (II) has been satisfactorily separated from the complex mixtures resulting from autoxidation. The latter process, on the other hand, is in harmony with the observed rise in the hydroxyl value (Tables 1, 3, 5, and 7), as found by the acetic anhydride–pyridine method.[19a] Thus, although it is highly probable

[17] Knight, Eddy, and Swern, *J. Amer. Oil Chemists' Soc.*, 1951, **28**, 188.
[18] Ellis, *J.*, 1950, 9; King, *J.*, 1951, 1980.
[19] O'Neill, " The Autoxidation of Drying Oils, II " (Technical Paper No. 155, The Research Assocn. of British Paint, Colour, & Varnish Manufacturers), 1948, (*a*) p. 19, (*b*) p. 37.

TABLE 4.

Approximate composition (%), calculated from Table 3, of the products obtained by autoxidising elaidic acid at 82° for 24 hr.

	(A)		(B)		(C)	
	(i)	(ii)	(i)	(ii)	(i)	(ii)
8- and 11-Oxoelaidic acids, $C_{18}H_{32}O_3$, deduced from (a) $E^{1\%}_{1\,cm.}$ at 224 mμ	3·4	4·1	5·6	10·6	2·1	2·0
8- and 11-Oxoelaidic acids, $C_{18}H_{32}O_3$, deduced from (b) hydrolysis	3·3	5·1	8·5	10·7	2·8	2·7
9,10-Ketol acids, as $C_{18}H_{34}O_4$	0·0	5·2	3·8	8·3	1·6	4·5
Other oxo-acids, as $C_{18}H_{32}O_3$	0·0	0·0	0·0	0·8	0·0	0·0
9,10-Epoxystearic acid	10·4	5·0	0·5	0·0	11·1	3·6
Hydroperoxyelaidic acids	9·1	0·2	25·7	0·2	0·6	0·04
9,10-Dihydroxystearic acid (combined)	3·7	5·7	6·8	6·1	0·2	7·5
Hydroxyelaidic acids	18·3	20·0	30·4	40·1	9·5	5·1
Other unsaturated products and unchanged elaidic acid, as $C_{18}H_{34}O_2$	50·3	53·7	10·7	18·8	70·8	77·8
Steam-volatile acids as nonanoic	4·6	4·0	5·8	6·0	1·5	2·0
Non-volatile, water-soluble acids, as azelaic	5·3	3·9	2·4	2·5	0·1	0·1
Neutral, steam-volatile oil, as $C_9H_{16}O$	0·5	0·4	1·2	1·8	0·2	0·3

TABLE 5.

Effect of heat on the products obtained by autoxidising methyl oleate at 50° for 12 days: (A) whole product; (B) fraction not forming urea complex; (C) fraction forming urea complex. (i) Before, (ii) after being heated under N_2 at 88° for 53 hr.

	(A)		(B)		(C)	
	(i)	(ii)	(i)	(ii)	(i)	(ii)
Physical condition of oil	Colourless, mobile	Very pale yellow	Pale yellow	Yellow, less mobile	Colourless	Very pale yellow
Reduction of Fehling's soln.	Slight	Trace	Slight	Moderate	None	None
Acid value (mg. KOH/g.)	12	21	18	52	1	1
Iodine value	63	61	58	62	65	64
$E^{1\%}_{1\,cm.}$ at 224 mμ	25	38	39	63	19	21
Neutral, steam-volatile oil (%)	1·1	1·1	1·2	2·4	1·1	1·1
Volatile oil (mainly nonanal and nonanone) resulting from hydrolysis on distn. with 0·5N-NaOH (%)	2·3	3·1	4·6	4·8	2·0	1·9
Nonanal on distn. of the residual solution from the above hydrolysis with KIO_4 at pH 8·0 (%)	0·6	1·0	1·2	1·6	0·5	0·4
Saponification value	220	208	254	220	200	199
Nonanal resulting from oxidn. with KIO_4 at pH 8·0 (%)	0·1	0·0	0·0	0·0	0·1	0·0
Carbonyl (%)	0·39	0·97	0·54	2·91	0·28	0·41
Oxiran-O (%)	0·08	0·14	0·00	0·00	0·24	0·29
Active O (%)	0·93	0·20	2·01	0·07	0·14	0·01
OH value (corrected for hydroperoxide and epoxide)	10	24	22	74	6	0
Steam-volatile acids, mequiv. (%)	25	26	52	75	8	10
Non-volatile, water-soluble acids, mequiv. (%)	10	12	16	25	1	1

that in the early stages of autoxidation the greater part of the αβ-unsaturated ketones originates from hydroperoxides by one or other of these routes, other pathways cannot be excluded. Spectroscopic and other evidence seems to suggest that, in the more advanced stages of autoxidation, peroxide decomposition gives a much smaller yield of αβ-unsaturated ketones (Table 9; cf. ref. 16). This may be connected with the heterogeneity of the peroxides, some part of which is thought to consist of monoxides of the Staudinger type,[4] but could also be due to progressive cyclisation to 1,2-dioxolans, which are known to give the usual iodide and titanium tests.[20]

In general, the total concentrations of (I) and (II), deduced from their neutral volatile hydrolysis products (nonanal and nonan-2-one), agree reasonably with those found by the

[20] See Criegee and Paulig, *Chem. Ber.*, 1955, **88**, 712.

Vol. 1961, page 4327, line 5 *. *For* monoxides *read* moloxides.

TABLE 6.

Approximate composition (%), calculated from Table 5, of the products obtained by autoxidising methyl oleate at 50° for 12 days.

	(A)		(B)		(C)	
	(i)	(ii)	(i)	(ii)	(i)	(ii)
Methyl 8- and 11-oxo-oleates, $C_{19}H_{34}O_3$, deduced from (a) $E^{1\%}_{1\,cm.}$ at 224 mμ	4·8	7·3	7·5	12·2	3·8	4·0
Methyl 8- and 11-oxo-oleates, $C_{19}H_{34}O_3$, deduced from (b) hydrolysis	6·0	7·7	11·7	12·0	5·2	5·1
9,10-Ketol-esters, $C_{19}H_{36}O_4$	0·6	0·0	0·0	0·0	0·4	0·1
Other oxo-esters, as $C_{19}H_{34}O_3$	0·0	1·3	0·0	15·4	0·0	0·0
Methyl 9,10-epoxystearate	1·5	2·7	0·0	0·0	4·7	5·6
Hydroperoxy-esters, as $C_{19}H_{36}O_4$	19·1	4·1	41·3	1·4	2·8	0·3
9,10-Dihydroxy-esters, as $C_{19}H_{38}O_4$	0·5	1·6	3·3	4·4	0·0	0·0
Hydroxyoleate esters, $C_{19}H_{36}O_3$	4·8	11·8	9·4	36·9	3·0	0·1
Other unsaturated products and unchanged methyl oleate, as $C_{19}H_{36}O_2$	46·9	47·8	14·6	10·2	66·7	70·9
Steam-volatile acids, as nonanoic	4·0	4·1	8·2	11·9	1·3	1·6
Non-volatile, water-soluble acids, as monomethyl azelaate	2·0	2·4	3·3	5·0	0·1	0·1
Neutral, steam-volatile oil	1·1	1·1	1·2	2·4	1·1	1·1

TABLE 7.

Effect of heat on the products obtained by autoxidising methyl oleate at 83° for 24 hr.: (A) whole product; (B) fraction not forming urea complex; (C) fraction forming urea complex. (i) Before, (ii) after being heated under nitrogen at 85° for 2 days.

	(A)		(B)		(C)	
	(i)	(ii)	(i)	(ii)	(i)	(ii)
Physical condition of oil	Nearly colourless	Very pale yellow	Very pale yellow	Pale yellow	Nearly colourless	Nearly colourless
Reduction of Fehling's soln.	Slight	Slight	Moderate	Moderate	None	None
Acid value (mg. KOH/g.)	24	30	33	63	3	4
Iodine value	48	48	49	53	50	50
$E^{1\%}_{1\,cm.}$ at 224 mμ	37	44	39	68	32	33
Neutral, steam-volatile oil (%)	1·5	1·5	2·1	2·3	1·1	1·1
Volatile oil (mainly nonanal and nonan-2-one) resulting from hydrolysis on distn. with 0·5N-NaOH (%)	2·6	3·4	3·7	4·8	3·0	3·1
Nonanal on distn. of the residual solution from the above hydrolysis with KIO_4 at pH 8·0 (%)	0·9	2·0	1·7	2·0	1·1	1·1
Saponification value	218	211	250	213	197	197
Nonanal resulting from oxidn. with KIO_4 at pH 8·0 (%)	0·0	0·1	0·0	0·0	0·0	0·1
Carbonyl (%)	0·68	1·19	0·96	2·69	0·45	0·52
Oxiran-O (%)	0·61	0·47	0·0	0·0	1·09	1·06
Active O (%)	0·82	0·28	1·81	0·20	0·14	0·07
OH value (corrected for hydroperoxide and epoxide)	35	47	42	74	13	11
Steam-volatile acids, mequiv. (%)	32	39	63	77	9	10
Non-volatile, water-soluble acids, mequiv. (%)	18	18	22	28	1	1

spectrophotometric method.[7] The discrepancies observed in the case of peroxide-enriched fractions [Tables 2, 4, 6, and 8; columns B(i)] may be attributed to secondary oxidative changes during alkaline hydrolysis. The presence of appreciable concentrations of βγ-unsaturated ketones in these fractions appears to be ruled out by the virtual absence of " other oxo-acids " (or esters) as calculated from the carbonyl content. However, significant amounts of carbonyl compounds of unknown constitution, in which the carbonyl group is presumably more remote from the double bond, result from heating peroxide-enriched fractions from methyl oleate [Tables 6 and 8; columns B(ii)]. These resist hydrolysis, and may contain some di- or poly-meric material.[21,10,7]

[21] Swern, Knight, Scanlan, and Ault, *J. Amer. Chem. Soc.*, 1945, **67**, 1132.

TABLE 8.

Approximate composition (%), calculated from Table 7, of the products obtained by autoxidising methyl oleate at 83° for 24 hr.

	(A)		(B)		(C)	
	(i)	(ii)	(i)	(ii)	(i)	(ii)
Methyl 8- and 11-oxo-oleates, $C_{19}H_{34}O_3$, deduced from (a) $E^{1\%}_{1\,cm.}$ at 224 mμ	7·1	8·6	7·5	13·3	6·2	6·3
Methyl 8- and 11-oxo-oleates, $C_{19}H_{34}O_3$, deduced from (b) hydrolysis	6·6	8·3	9·0	11·5	7·5	7·6
9,10-Ketol-esters, $C_{19}H_{36}O_4$	0·0	0·6	0·0	0·0	0·0	0·3
Other oxo-esters, as $C_{19}H_{34}O_3$	0·0	1·1	0·0	12·1	0·0	0·0
Methyl 9,10-epoxystearate	12·0	9·2	0·0	0·0	21·3	20·8
Hydroperoxy-esters, as $C_{19}H_{36}O_4$	16·8	5·7	37·2	4·1	2·9	1·4
9,10-Dihydroxy-esters, as $C_{19}H_{38}O_4$	0·7	3·5	4·7	5·3	0·8	0·7
Hydroxyoleate esters, $C_{19}H_{36}O_3$	19·0	22·3	19·0	36·2	6·3	5·1
Other unsaturated products and unchanged methyl oleate, as $C_{19}H_{36}O_2$	16·0	21·0	0·0	0·0	44·0	46·0
Steam-volatile acids, as nonanoic	5·1	6·2	10·0	12·2	1·4	1·5
Non-volatile, water-soluble acids, as monomethyl azelaate	3·6	3·6	4·4	5·7	0·2	0·2
Neutral, steam-volatile oil	1·5	1·5	2·1	2·3	1·1	1·1

TABLE 9.

Effect of heat on peroxide-enriched fractions from methyl oleate after autoxidation at 80° for (a) 10 hr., (b) 60 hr. (i) Before, (ii) after being heated under N_2 at 80° for 2 days.

	(a)		(b)	
	(i)	(ii)	(i)	(ii)
Active O (%)	1·55	0·07	1·11	0·09
$E^{1\%}_{1\,cm.}$ at 224 mμ	50	77	38	42
8- and 11-Oxo-oleic esters (%)	9·7	14·9	7·4	8·1
Carbonyl (%)	1·19	2·42	1·26	1·98
Iodine value	62	64	27	35

Fractions enriched in peroxides by the urea-complex method contain little or no epoxide before or after being heated under nitrogen, while the whole products (columns A) usually suffer some reduction of epoxide content and increase of dihydroxystearic acid derivatives when heated (cf. refs. 22 and 10). The absence of any appreciable epoxide formation or double-bond scission during the heating process is supported by the relatively constant iodine value, the accuracy of which as determined by Wijs's method (1 hr.) does not appear to be seriously affected by the presence of moderate concentrations of peroxides.[23,19b] In an independent experiment, no expoxide was found after methyl oleate had been heated with 50% t-butyl hydroperoxide in t-butyl alcohol at 85° for 2 days. The 9,10-epoxystearic acid in autoxidised oleic or elaidic acid is predominantly the *trans*-form,[24] and has also been separated from autoxidised n-propyl oleate following saponification.[25] This oxide, but not the *cis*-isomer, has now been isolated similarly from autoxidised methyl oleate. A free-radical mechanism has been suggested[17] to explain the formation of the *trans*-oxide from oleate by way of hydroperoxides, involving an inversion of configuration, but the present work suggests that this oxide is not a primary product of either hydroperoxide decomposition or the action of hydroperoxides on unchanged olefin.

The increase in the hydroxyl value when the autoxidation products of elaidic acid or oleic esters are heated is most marked with the peroxide-enriched fractions from methyl

[22] Nicolet and Poulter, *J. Amer. Chem. Soc.*, 1930, **52**, 1186; Deatherage and Mattill, *Ind. Eng. Chem.*, 1939, **31**, 1425.
[23] Hamilton and Olcott, *Ind. Eng. Chem.*, 1937, **29**, 217; Farmer and Sutton, ref. 11; cf. Coleman, Knight, and Swern, ref. 2.
[24] Ellis, *Biochem. J.*, 1936, **30**, 753.
[25] Feuell and Skellon, *J.*, 1954, 3414.

XUM

oleate, in which it is clearly due to the formation of simple hydroxy-derivatives. In autoxidised elaidic acid this increase arises in part from the formation of ketols and, in certain instances, dihydroxy-derivatives (Tables 2 and 4; columns A and C), but peroxide-rich fractions (columns B) may show a loss of dihydroxy-derivatives on heating, perhaps as a result of their further oxidation to ketols and the virtual absence of epoxides from which they may be formed. The uncatalysed autoxidation of methyl oleate gave little or no ketol esters (cf. Skellon [8]).

Surprisingly little increase of acidity occurs when peroxide-enriched fractions of autoxidised elaidic acid are heated under nitrogen, but similar fractions from methyl oleate show a significant increase in acid value and a corresponding fall in saponification value (Tables 5 and 7; columns B), consistent with ester hydrolysis, without chain scission at the double bond. Autoxidised ethyl oleate was found to resemble autoxidised methyl oleate closely in this and other respects, and detailed analyses have therefore been omitted. Incidental work on the precipitation of urea complexes under prescribed conditions is summarised in the Experimental section.

The available evidence suggests, therefore, that the principal secondary products arising from hydroperoxide decomposition during the early stages of autoxidation are hydroxy-compounds and αβ-unsaturated ketones. The peroxides in autoxidised elaidic acid lead in addition to ketols and to unsaturated compounds which are probably oxygen-bonded, but contain no other functional group. Peroxide-rich fractions from oleic esters, however, yield carbonyl compounds in which the carbonyl group is more remote from the double bond and which may be partly dimeric, but these do not appear in significant amounts in the whole autoxidation products during the early stages of autoxidation.[7] Peroxide decomposition does not result in extensive double-bond scission or epoxide formation under the conditions described.

Experimental

Materials.—Elaidic acid, recrystallised successively from acetic acid and ethanol, had m. p. 44·5°. Methyl oleate, after two fractionations, had b. p. 200—204°/13·5 mm. (Found: Iodine value, 84·4; Sap. value, 190. Calc. for $C_{19}H_{36}O_2$: Iodine value, 85·6; Sap. value, 189). Ethyl oleate similarly had b. p. 220—222°/19° (Found: Iodine value, 80·5; Sap. value, 180°. Calc. for $C_{20}H_{38}O_2$: Iodine value, 81·8; Sap. value, 181).

Methods.—Except as mentioned below, these were as previously described.[7,16]

Neutral, Steam-volatile Oil from Autoxidised Oleic Esters.—The autoxidised ester (2 g.), or fraction obtained from it by the urea method, was shaken with water (100 ml.) and sufficient 0·1N-sodium hydroxide, as calculated from the acid value, to bring the pH to 8·0. Distillation into a special trap [27] gave a volatile oil, which afforded a 2,4-dinitrophenylhydrazone, m. p. 80—92° (Found: N, 17·45. Calc. for $C_{15}H_{22}N_4O_4$: N, 17·4%), shown by paper chromatography to be a mixture of nonan-2-one and nonanal derivatives. The volatile oil sometimes contained a small amount of unchanged methyl or ethyl oleate, due to the slight steam-volatility of the esters.

8- *and* 11-*Oxo-oleic Esters.*—The spectrophotometric determination was based on an $\varepsilon_{max.}$ value of 16,000 at 224 mμ for these esters in ethanol, *i.e.*, $E^{1\%}_{1\ cm.}$ 516 for methyl oleate, 493 for ethyl oleate. All measurements were made with a Unicam S.P. 500 spectrophotometer.

Periodate Oxidation of the Autoxidised Esters.—Oxidation with periodate at pH 8·0 afforded a steam-volatile oil whose 2,4-dinitrophenylhydrazone crystallised in orange-yellow plates, m. p. 95—100° (Found: N, 17·7%), shown by paper chromatography to be mainly the nonanal derivative, with traces of octanal derivative.

Carbonyl.—A pH meter was used, titrations being taken to pH 3·7.

Hydroxyl Value (cf. ref. 19*a*).—The substance (about 1 g.) was heated under reflux with a 20% solution of acetic anhydride ("AnalaR") in ordinary pyridine (5 ml.) on a water-bath for 2 hr. Water (5 ml.) was then added, and heating continued for a further 5 min. The solution

[26] Cf. Swern, Witnauer, and Knight, *J. Amer. Chem. Soc.*, 1952, **74**, 1655.
[27] King, *Nature*, 1953, **171**, 566.

was rapidly cooled, ethanol (25 ml.) and phenolphthalein (10 drops of 1% solution) were added, and the solution was titrated with methanolic potassium hydroxide. A blank was carried out simultaneously, omitting only the test substance.

The following corrections were applied: (*a*) For active oxygen. Hydroperoxides of the type found in autoxidised fats react under these conditions to the extent of about 50% of the theoretical;[28] hence an amount equal to 17·5 × % active oxygen was subtracted from the apparent hydroxyl value.

(*b*) For epoxides. *trans*-9,10-Epoxystearic acid was shown to react to the extent of 10% of the theoretical, hence 7·0 × % oxiran-oxygen was subtracted.

The concentration of hydroxyelaidic acid or hydroxyoleic ester was calculated from the corrected hydroxyl value, allowances having been made for the 9,10-ketols (1·784 × % ketol-stearic acid) and dihydroxy-compounds (1·772 × % dihydroxystearic acid), the latter being assumed to be in the monoacylated form.[7]

Fractionation by the Urea-complex Method.—The following procedure was typical. Methyl oleate (60 g.) was autoxidised at 83° for 24 hr. with a rapid stream of oxygen. Two samples, A(i) and A(ii) (each of about 10 g.), were withdrawn, and the remainder of the product was poured into a hot solution of urea (230 g.) in methanol (650 ml.) with stirring. The mixture was set aside for 30 min., cooled at room temperature for 2 hr., and filtered. The crystalline complex was decomposed by stirring with water (1 l.), and the resulting oil (26·5 g.) was isolated by ether extraction and divided into two parts, C(i) and C(ii). The filtrate from the urea complex was diluted with water (2 l.), and saturated sodium sulphate solution (400 ml.), and extracted with ether. Removal of the solvent at room temperature under reduced pressure left a pale yellow oil (15 g.), which was divided into two parts, B(i) and B(ii). Fractions A(ii), B(ii), and C(ii) were heated under nitrogen in stoppered tubes at 85° for 2 days, and all fractions were then analysed.

Isolation of trans-9,10-*Epoxystearic Acid from Autoxidised Methyl Oleate.*—The crystalline urea complex obtained from methyl oleate (50 g.) which had been autoxidised at 80° for 2 days was decomposed with water (1 l.), and the resulting oil (23 g.) was hydrolysed by boiling it gently with 0·5N-sodium hydroxide (400 ml.) in an open vessel for 2 hr. to remove volatile products. Acidification of the cooled solution gave a semi-solid, which was resolved by filtration into an oil and a fatty solid (5 g.), containing a little dihydroxystearic acid, m. p. 130°, and fatty acids. The former was shaken with light petroleum (100 ml.; b. p. 40—60°) and water (50 ml.) in a separator and left overnight. A small deposit of *threo*-dihydroxystearic acid, m. p. 92°, was removed by filtration, and the dried petroleum layer was concentrated to about 30 ml. and cooled at 0° overnight. The precipitate of crude elaidic acid oxide (0·75 g.) was recrystallised successively from light petroleum and ethanol, and gave the pure epoxide (0·5 g.), m. p. 55·5°, not depressed by an authentic specimen. Hydrolysis of the oxide was best effected by refluxing it for 1 hr. with acetic acid (2·5 ml.), followed by dilution with water (12·5 ml.), and further refluxing with 40% sodium hydroxide solution (9 ml.) for 1 hr. Dilution and acidification then gave *erythro*-dihydroxystearic acid, which crystallised from ethanol in plates (0·47 g.), m. p. 132°.

Urea Complexes.—The addition of saturated methanolic urea (10 ml.) to the pure substance (0·1—0·2 g.) in methanol (1 ml.) at room temperature gave a crystalline precipitate of inclusion compound within 2 hr, with oleic or elaidic acid and their methyl or ethyl esters, the 9,10-epoxystearic acids, *trans*-11-oxoheptadec-9-ene-1-carboxylic acid, 12-oxoelaidic acid (incomplete), undecan- or decan-2-one, and nonan-2-one (incomplete), but not with the 9,10-dihydroxy-,[26] acetoxyhydroxy-, or hydroxyoxo-stearic acids, ricinoleic, nonanoic, or azelaic acid, octan-2-one, octanal, or nonanal (some oil separated).

The author thanks Professor R. T. Williams for his interest throughout this work.

Department of Biochemistry,
St. Mary's Hospital Medical School,
London, W.2.

[*Received, March 28th,* 1961.]

[28] O'Neill, Ref. 19, pp. 23, 24.

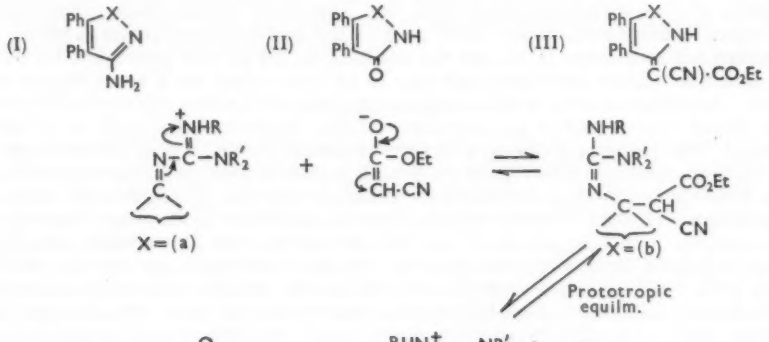
XUM

854. ***Heterocyclic Derivatives of Guanidine. Part III.*[1] *Stoicheiometry and Kinetics of the Condensation of Ethyl Cyanoacetate with Guanidino-2H-pyrroles.***

By J. E. Banfield.

Guanidines are displaced in the above reactions by a nucleophilic addition followed by prototropic changes and an elimination. The kinetics are complex, the order in ethyl cyanoacetate being non-integral, and an interpretation based upon a rate-determining elimination step is presented.

Previous attempts (not reported) to establish the stoicheiometry of the reaction [2] of 5-guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole [represented in formula I; X = (a); R = R′ = H; by one of its tautomeric forms [2]] with ethyl cyanoacetate by accounting for the atoms of the guanidino-residue were abortive. However, application of methods found successful in another problem to the analogous reaction of the piperidine analogue [I; X = (a); R = H; NR_2' = piperidino] with ethyl cyanoacetate in acetic acid now establish that 1-amidinopiperidine is formed along with the compounds [II and III; X = (d)]; compound [II; X = (d)] had not earlier [1] been detected in the reaction of these components in the absence of acetic acid; its formation is attributed to partial hydrolysis of the imino-compound to the lactam [II; X = (a); R = H, NR_2' = piperidino]. Reaction of this with ethyl cyanoacetate in acetic acid gave 1-amidinopiperidine.



Scheme (a)

Accordingly, in view of the evolution of ammonia noted [2] when 2-imino-3,4-diphenyl-5-oxo-3-pyrroline reacted with ethyl cyanoacetate, it seemed likely that ammonia and/or the guanidine is displaced in a nucleophilic reaction of the protonated pyrrole derivative by (presumably) the cyanoacetate carbanion or enol. Qualitative attempts to demonstrate basic catalysts in these reactions by addition of an excess of sodium acetate to the above mixtures were not successful; apparent lack of basic catalysis might suggest participation

[1] Part II, *J.*, 1961, 2098.
[2] Part I, *J.*, 1960, 2108.

of the enol or anion of ethyl cyanoacetate in an aldol condensation mechanism [3] as exemplified in scheme (a).

Preliminary attempts to follow the kinetics of the above reactions were not encouraging until a compound [II; X = (a); R = Me, R′ = Me] was prepared in the course of another investigation (cf. the Experimental section). Although the ultraviolet absorption of the oxopyrrole is of similar character to that of known compounds of this type, it is distinguished from them by being hypsochromically displaced, thus more readily permitting spectroscopic study of the kinetics of its reaction with ethyl cyanoacetate. Further, this oxopyrrole was soluble in ethanol (unlike some of the compounds described earlier) to a convenient degree. The reaction was rather slow, except at or near the boiling point of ethanol, and therefore was followed under reflux, although with some resultant loss of precision; some runs at 66° gave good first-order coefficients but were inconveniently slow.

Experimental

Reaction of 1-N′-(2-*Oxo*-3,4-*diphenyl*-2H-*pyrrol*-5-*yl*)*amidinopiperidine Nitrite with Ethyl Cyanoacetate.*—A mixture of this salt (1·0 g.), ethyl cyanoacetate (0·7 ml.), and acetic acid (2 ml.) was refluxed for 2 hr., diluted with methanol, and cooled, to yield 2-(α-cyano-α-ethoxycarbonylmethylene)-5-oxo-3,4-diphenyl-3-pyrroline (0·25 g.) which (from ethanol) had m. p. 165—169°. The mother-liquor was basified with sodium carbonate and treated with sodium picrate, giving 1-amidinopiperidine picrate, m. p. 151—152° (Found: C, 40·5; H, 4·8. Calc. for $C_{12}H_{16}N_6O_7$: C, 40·45; H, 4·5%).

Reaction of 1-N′-(2-*Imino*-3,4-*diphenyl*-2H-*pyrrol*-5-*yl*)*amidinopiperidine with Ethyl Cyanoacetate.*—The pyrrole (2·0 g.) gave, by the above method (½ hour's refluxing), 2,5-di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-3-pyrroline (1·5 g.), m. p. and mixed m. p. 253—254·5° (from butan-1-ol), and 1-amidinopiperidine picrate (1·3 g.), m. p. 251—253° (Found: C, 40·6; H, 4·7%). The mother-liquors gave a solid (0·3 g.) which by chromatography on alumina afforded 2-(α-cyano-α-ethoxycarbonylmethylene)-5-oxo-3,4-diphenyl-3-pyrroline (0·19 g.), m. p. 163—164° (Found: C, 73·0; H, 4·65; N, 8·6. Calc. for $C_{21}H_{16}N_2O_3$: C, 73·2; H, 4·7; N, 8·1%).

2-*Cyanomethylene*-5-*oxo*-3,4-*diphenyl*-3-*pyrroline.*—2-α-Cyano-α-ethoxycarbonylmethylene-5-oxo-3,4-diphenyl-3-pyrroline (0·4 g.) was warmed to 30° with ethanolic-aqueous sodium hydroxide. The mixture, set aside for 2 days and then acidified, gave the *nitrile* (134 mg.), m. p. 197·5—198·5° (from ethanol), which when dried at 150°/0·01 mm. lost less than 2% by weight (Found: C, 79·3; H, 4·46; N, 10·2; O, 6·4. $C_{18}H_{12}N_2O$ requires C, 79·4; H, 4·4; N, 10·3; O, 5·9%), $\lambda_{max.}$ 318 mμ (log ε 4·419 in EtOH).

2-*Imino*-3,4-*diphenyl*-5-NNN′-*trimethylguanidino*-2H-*pyrrole.*—*NNN′*-Trimethylguanidinium sulphate was prepared from *NS*-dimethylisothiouronium sulphate and dimethylamine and afforded the picrate, m. p. 150·5—152° (lit., 151—152°). This sulphate (6·3 g.), sodium (0·9 g.), and *trans*-αβ-dicyanostilbene (7 g.) yielded, by the general method [3] after several days at 50° and then at room temperature, a yellow solution which on evaporation gave a brown oil. This was taken up in benzene and then yielded the crude pyrrole (7·0 g.). Recrystallisation of this from hot solvents caused decomposition unless the time of heating was kept at a minimum: even so slight colour developed. From acetone the *pyrrole* separated in yellow needles, m. p. 210° (decomp.) (Found: C, 72·05; H, 6·3; N, 20·2. $C_{20}H_{21}N_5$ requires C, 72·5; H, 6·4; N, 21·1%). From ethyl methyl ketone it was obtained in yellow prisms, m. p. 209° (decomp.) (Found: C, 72·1; H. 6·2; N, 20·5%). In 95% ethanol it had $\lambda_{max.}$ 304, $\lambda_{infl.}$ 354, 237, 227 mμ (log ε 4·288, 3·28, 4·24, 4·30) changed by acetic acid to $\lambda_{max.}$ 303, $\lambda_{infl.}$ 357, 250 mμ (log ε 4·262, 3·28, 4·08); both spectra are of type E.[2]

2-*Oxo*-3,4-*diphenyl*-5-NNN′-*trimethylguanidino*-2H-*pyrrole.*—The foregoing 2-imino-compound (1·5 g.) in ethanolic-aqueous acetic acid was treated with sodium nitrite (4 g.) and the product refrigerated for 2 months, filtered from a trace of green solid, and basified with sodium hydroxide solution, giving the *dihydrate*, m. p. 252° (decomp.), of the oxopyrrole (Found: C, 64·1; H, 6·4; N, 14·75. $C_{20}H_{20}N_4O,2H_2O$ requires C, 65·2; H, 6·6; N, 15·2%). This, recrystallised from ethanol, afforded the *oxopyrrole* in yellow prisms, m. p. 258—259° (decomp.) (Found: C, 72·2;

[3] (*a*) Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 284; (*b*) Barton, McCapra, May, and Thudium, *J.*, 1960, 1298.

XUM

H, 6·0; N, 16·5, 17·0; O, 5·5. $C_{20}H_{20}N_4O$ requires C, 72·3; H, 6·1; N, 16·9; O, 4·8%), $\lambda_{max.}$ 298, 230, $\lambda_{infl.}$ 340 mμ (log ε 4·309, 4·300, 3·32 in 95% EtOH), changed by alkali to $\lambda_{max.}$ 299, $\lambda_{infl.}$ 340, 228 mμ (log ε 4·314, 3·41, 4·33) (both of type E[2]) and by acetic acid to $\lambda_{max.}$ 360, 277, $\lambda_{infl.}$ 250 mμ (log ε 3·738, 4·196, 4·133) (type I[2]).

The oxopyrrole was heated in ethyl cyanoacetate, giving 2-α-cyano-α-ethoxycarbonylmethylene-5-oxo-3,4-diphenyl-3-pyrroline, m. p. and mixed m. p. 169—170° (from ethanol).

Kinetic Experiments.—Materials. Ethanol was dried by refluxing it with sodium ethoxide and diethyl phthalate and was then fractionally distilled. In some experiments, where rigorous dryness was not maintained, ethanol (commercial, absolute) was purified by fractionation. Triethylamine was fractionated from sodium.

Toluene-*p*-sulphonic acid was prepared from the monohydrate by dehydration at 100° under reduced pressure, then under an oil-pump vacuum, and was then made up in ethanol and standardised alkalimetrically.

Sodium ethoxide solution was freshly prepared and was standardised acidimetrically after dilution with water.

The oxopyrrole was made up in ethanol and aliquot parts of a stock solution were used.

Method. 2-Oxo-3,4-diphenyl-5-*NNN'*-trimethylguanidino-2*H*-pyrrole, ethyl cyanoacetate, and any additional materials were measured volumetrically, made up to 50·0 ml., and placed in a flask fitted with a ground-glass stopper, reflux condenser, stoppered side arm, and protecting tube, all of which had been kept at 115° overnight before assembly. When the solution was refluxing and was adjudged to have reached dynamic equilibrium (thermal), a sample was removed and cooled, and its optical density was measured on a Unicam S.P. 500 spectrophotometer (at least three readings; D usually $\pm 0{\cdot}001$). Further samples were removed and measured at timed intervals. Temperatures measured with a thermometer immersed in the boiling liquid varied from 78·8° to 80·2°; in the Tables the values 79·5° is arbitrarily given. Runs at 66·05° were carried out conventionally in stoppered flasks.

TABLE 1. *First-order rate coefficients (min.$^{-1}$) of the reaction between ethyl cyanoacetate* (CA), *and 2-oxo-3,4-diphenyl-5-NNN'-trimethylguanidino-*2H*-pyrrole* (OP) *in ethanol.*

Run	Temp.	10^3[OP]	10^3[CA]		10^3k_1 (obs.)	10^3k_1 (calc.)	R[f]
16	79·5°	5·22	752		5·31	5·55	4·83
9	,,	13·1	376		4·50	4·85	4·18
12	,,	5·22	,,		3·94	3·93	,,
8	,,	2·61	,,		3·77	3·88	,,
10	,,	13·1	188	[a]	3·00	3·20	3·37
7	,,	,,	,,	[a]	3·11	3·13	,,
55	,,	10·89	,,		3·34	3·36	,,
11	,,	13·1	94	[a]	2·12	2·07	2·32
13	,,	,,	37·6	[a]	1·41	1·29	1·23
56	,,	10·89	,,		1·39	1·46	,,
14	,,	13·1	15·1		1·08	0·97	0·57
59	,,	10·89	,,		1·46	1·36	,,
15	,,	13·1	7·5	[a]	0·824	0·815	0·30
60	,,	10·89	—		—	0·000	
65	66·0$_5$	10·89	752		2·44	2·41	
57	,,	,,	188		0·908	0·91	
66	,,	,,	75·2		0·493	0·493	
58	,,	,,	37·6		0·366	0·368	
61	,,	,,	7·5		0·28	0·24	
62	,,	,,	—		—	0·000	
25	79·5	5·22	376		—	0·000	
17	,,	,,	188	[c]	2·6	—	
21	,,	,,	,,	[d]	2·45	2·6	
24	,,	,,	,,	[e]	2·68	—	
23	,,	2·61	,,	[e]	2·62	—	

[a] Runs in fractionated ethanol; other runs were in phthalate-dried ethanol, no significant difference being noted between the two sets. [b] Contained toluene-*p*-sulphonic acid (0·0019M); for other concentrations of acid see Fig. 1. [c] In ethanol containing 4% of water; the initial rate is given; however, the rate decreased rapidly to a very low value. The final solution from this run had an ultraviolet absorption curve closely resembling that of the oxopyrrole in acetic acid ($\lambda_{max.}$ 276, 347 mμ; log ε 4·25, 3·95); the decrease in rate is ascribed to production of acid by hydrolysis of the ethyl cyanoacetate. [d] Contained 0·2% (volume) of aqueous 0·024M-sodium hydroxide. [e] Contained 0·145M-triethylamine. [f] $1/R = 175 + 24/[CA]$, the equation derived from the line of Fig. 3.

For 2-α-cyano-α-ethoxycarbonylmethylene-5-oxo-3,4-diphenyl-3-pyrroline in ethanol, log $\varepsilon_{364} = 4{\cdot}313$. Figures for a typical run (No. 13, Table 1, where details of concentrations, etc., can be found) are:

Optical density	0·271	0·293	0·333	0·360	0·397	0·426	0·457	0·490	0·524	0·551
Time (min.)	0	10	20	30	40	50	60	70	80	90
10^3k_1 (min.$^{-1}$)	—	0·90	1·29	1·24	1·33	1·32	1·33	1·34	1·37	1·36

Although initial readings tended to be erratic, good first-order plots were obtained for most of the runs; however, average calculated k_1 values are appended, as variation of these from the graphical values is a measure of the precision of the results, probably ±5%.

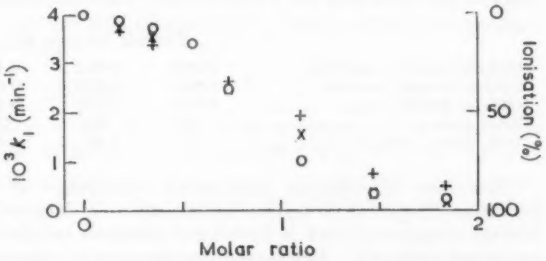


FIG. 1. *First-order rate coefficients for the reaction of ethyl cyanoacetate with 2-oxo-3,4-diphenyl-5-NNN′-trimethylguanidino-2H-pyrrole* (○) *in the presence of varying molecular amounts of toluene-p-sulphonic acid; and the degree of protonation of the pyrrole by the acid under comparable conditions, measured both at* 310 mμ (×) *and at* 370 mμ (+).

FIG. 2. *Reaction of ethyl cyanoacetate with sodium ethoxide* (□) *and with sodium ethoxide and 2-oxo-3,4-diphenyl-5-NNN′-trimethylguanidino-2H-pyrrole* (○) *under conditions summarised in Table 2.* (*Run nos. denoted on curves.*)

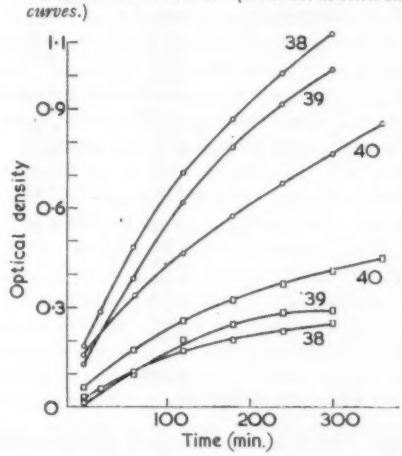
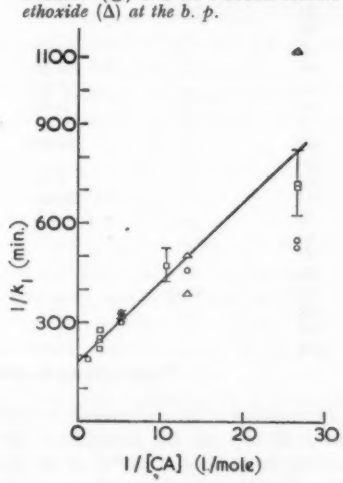


FIG. 3. *Reciprocals of the first-order rate coefficients for the reaction of ethyl cyanoacetate with 2-oxo-3,4-diphenyl-5-NNN′-trimethylguanidino-2H-pyrrole as a function of the reciprocal of the total concentration of the former in ethanol* (□), *in ethanolic* 0·00037M-*sodium ethoxide* (○) *and in* 0·0092M-*sodium ethoxide* (Δ) *at the b. p.*



Infinity run. A mixture of the oxopyrrole (5·00 ml. of $2{\cdot}61 \times 10^{-5}$M-solution), ethyl cyanoacetate (1 ml.) and ethanol was refluxed for 17 hr., cooled, and made up to 50·0 ml. with ethanol, and the optical density at 364 mμ was determined (Found: *D*, 0·537. Calc.: *D*, 0·537). The absorption of the solution in the range 310—420 mμ was within ±0·01 in log ε of that of a pure specimen of 2-α-cyano-α-ethoxycarbonylmethylene-5-oxo-3,4-diphenyl-3-pyrroline and showed only slight deviations outside this range.

Effect of sodium ethoxide. All these experiments were carried out with rigorously dried apparatus and with phthalate-dried ethanol. Preliminary runs with 0·0093M-sodium ethoxide

gave rapidly increasing first-order coefficients, and the optical densities eventually exceeded the calculated infinity values. Thereafter the densities increased steadily and the solution obtained after several days was red and had a very high absorption at *ca.* 270 mμ; study of this reaction is in hand. Accordingly blank runs were carried out for each concentration of sodium ethoxide and for each concentration of ethyl cyanoacetate used, and the optical densities of runs with the oxopyrrole were corrected accordingly. Fig. 2 gives examples of optical density–time plots for the total and control runs. In spite of the large correction (as much as 50% as in run 40), good first-order plots were obtained as for run 47 (for concentrations, etc., see Table 2); corrections were greater for high ethoxide concentrations and for low ethyl cyanoacetate concentrations (pH-dependent) and were negligible for $<0{\cdot}0004$M-sodium ethoxide provided that the concentration of the ethyl cyanoacetate exceeded 0·035M.

Details for run 47.

Optical density, reaction	0·164	0·312	0·449	0·579	0·708	0·798
Optical density, control	0·005	0·023	0·041	0·048	0·050	0·056
Optical density, corr.	0·159	0·289	0·408	0·531	0·658	0·742
Time (min.)	0	60	120	182	250	300
10^3k_1 (corr.; min.$^{-1}$)	—	1·08	1·06	1·08	1·10	1·09

Acid–Base Equilibrium Experiments.—Ionisation of 2-oxo-3,4-diphenyl-5-NNN′-trimethylguanidino-2H-pyrrole in various concentrations of toluene-p-sulphonic acid. Solutions to contain the oxopyrrole ($5{\cdot}44 \times 10^{-5}$M) and toluene-*p*-sulphonic acid were made up to 25·0 ml. with fractionated ethanol. Fractions of the oxopyrrole ionised for various molar ratios of the acid, determined at two wavelengths, are given in Fig. 1.

TABLE 2. *Corrected first-order rate coefficients (min.$^{-1}$) of the reaction between ethyl cyanoacetate* (CA), *and 2-oxo-3,4-diphenyl-5-NNN′-trimethylguanidino-2H-pyrrole* (OP) *in ethanol containing sodium ethoxide.*

Run	Temp.	10^3[OP]	10^3[CA]	10^4[NaOEt]	10^3k_1	R †
38	79·5°	5·44	376	92·6	4·15	4·18
39	,,	,,	188	,,	2·99	3·37
42	,,	10·89	,,	,,	3·28	,,
41	,,	5·44	75·2	,,	2·64 *	2·02
43	,,	10·89	,,	,,	1·99 *	,,
40	,,	5·44	37·6	,,	0·89	1·23
44	,,	,,	192	3·70	3·22	3·33
63	,,	10·89	75·2	,,	2·18	2·02
46	,,	,,	38·4	,,	1·90	1·25
45	,,	5·44	,,	,,	1·82	,,
54	,,	10·89	8·3	,,	1·52	0·33
51	,,	,,	3·8	,,	1·33	
48	,,	,,	2·3	,,	1·28	
47	,,	,,	0·75	,,	1·08	
64	,,	,,	0	,,	0·00	
52	66·0$_5$	,,	376	,,	1·56	
49	,,	,,	189	,,	0·86	
50	,,	,,	76·0	,,	0·58	
53	,,	,,	38·4	,,	0·426	

* Corrections by interpolation. † $1/R = .175 + 24/[\text{CA}]$.

Protonation of the oxo-pyrrole by ethyl cyanoacetate. Solutions containing (i) the oxopyrrole ($5{\cdot}44 \times 10^{-5}$M), (ii) the oxopyrrole ($5{\cdot}44 \times 10^{-5}$M) and ethyl cyanoacetate (0·377M), and (iii) the oxopyrrole ($5{\cdot}44 \times 10^{-5}$M) in an excess of ethanolic toluene-*p*-sulphonic acid (0·002M), were used. Results are tabulated:

	(i)	(ii)	(iii)
Optical density at 310 mμ	0·743	0·694	0·281
Optical density at 330·5 mμ (an isosbestic point)	0·232	0·233	0·233
Optical density at 370 mμ	0·078	0·100	0·264

The proportion of oxopyrrole protonated in solution (ii) is 11% (measurement at 310 mμ) or 12% (measurement at 370 mμ).

Acidity of ethyl cyanoacetate. A stock solution containing sodium ethoxide ($1{\cdot}85 \times 10^{-2}$M) and a convenient concentration of phenolphthalein was prepared. Aliquot parts (5·00 ml.)

were added to various amounts of ethyl cyanoacetate (CA) and made up to 10·0 ml. with ethanol, the optical densities being determined (1 cm. stoppered cells) at 564 mμ; these densities

10^3[CA] ...	377	151	75·5	37·7	30·2	22·6	15·1	11·3	9·4	7·6	7·2	6·8	6·4
f	0·027	0·096	0·226	0·426	0·522	0·653	0·786	0·863	$0·92_3$	$0·97_4$	$0·97_4$	$0·99_8$	$0·99_6$
r	1·1	1·6	2·1	2·1	2·5	2·7	2·3	1·4	—	—	—	—	—

drifted slightly with time and were measured after *ca.* 5 min. The ratio $D_{sol.}/D_{[CA]=0} = f$ is given below. It is apparent that the ethoxide concentration cannot be ignored. Nevertheless the ratio

$$r = K_{ind.}/K_{CA} = f([CA] - [NaOEt])/(1 - f) \,.\, [NaOEt]$$

is given; thus the acid dissociation constant $K_{ind.}$ of phenolphthalein in ethanol is approximately twice that of ethyl cyanoacetate (K_{CA}).

Discussion

The mechanism proposed by Patai *et al.*[4] for the condensation of active methylene compounds with aldehydes—namely, either a rate-determining ionisation for malononitrile (in water) or a rate-determining second-order reaction of the enolate of ethyl cyanoacetate, diethyl malonate, or malononitrile in ethanol with the aldehyde—may account for their observations (but see below) but is inapplicable to our results. In the present instance the order in ethyl cyanoacetate is non-integral and decreases with increasing cyanoacetate concentration. First-order kinetics affected to a smaller extent in this way by subsequent steps have been discussed;[5] however an alternative explanation—a pre-equilibrium condensation step, with the concentration of the intermediate appreciable and a later rate-determining reaction—is considered a more reasonable explanation in this case.

The virtual independence of the rate (except at very low ethyl cyanoacetate concentrations) of added base excludes a rate-determining base-catalysed ionisation or bimolecular elimination step, whereas the near-stoicheiometric inhibition of the reaction by acid, which parallels the spectroscopically determined ionisation of the oxopyrrole (Fig. 1; determined for toluene-*p*-sulphonic acid under conditions closely comparable with those in the kinetic runs), indicates that the reactive molecular species is of the same net-charge type as that of the oxopyrrole. The mechanism proposed in scheme (*a*) on chemical grounds is thus qualitatively supported and the rate-determining step identified (probably) as the elimination step (c) ⟶ (d), the alternative[6] [isomerisation (b) ⟶ (c)] being expected to be fast as for the ionisation of ethyl cyanoacetate. It being of interest to establish that such a scheme is in quantitative accord with the results, the following simplified analysis for runs in the presence of significant concentration of sodium ethoxide was undertaken in which hydrolysis (ethanolysis; in the ionic sense) of ethyl sodiocyanoacetate is neglected. The concentration of the ethyl cyanoacetate anion is taken equal to that of the sodium ion. The activity coefficients (which however may be as high as 400 for charged species in ethanol[7]) are neglected; the ethyl cyanoacetate concentration being usually more than 100 times that of the oxopyrrole, the following equations then apply:

$$[NaOEt]_{added} = [CA^-]$$

$$[CA] = [CA]_{added} - [NaOEt]_{added}$$

We write [OP] and [OPH^+] for the actual concentrations of the oxopyrrole and its

[4] Patai and Israeli, *J.*, 1960, (*a*) 2020, (*b*) 2025; (*c*) Patai and Zabicky, *J.*, 1960, 2030; (*d*) Patai Zabicky, and Israeli, *J.*, 1960, 2038.

[5] (*a*) Bird, Hughes, and Ingold, *J.*, 1954, 634; (*b*) Bunton, Greenstreet, Hughes, and Ingold, *J.*, 1954, 647.

[6] Noyce, Pryor, and Bottini, *J. Amer. Chem. Soc.*, 1955, **77**, 1402; Noyce and Reed, *ibid.*, 1958, **80**, 5539.

[7] Bates, "Electrometric pH Determinations," Wiley, New York, 1954, p. 136.

XUM

protonated form, respectively; [PCA] = the concentration of the intermediate [I; X = (b); R = Me, R′ = Me]; [G] = the concentration of the guanidinium enol ion [I; X = (c); R = Me, R′ = Me]; [G^-] that of its anion ($G - H^+$); p = total concentration of all forms of the oxopyrrole added initially, or not converted into the product [II; X = (d)] at subsequent times.

Equilibrium constants are defined as follows:

$$[CA^-][H^+] = K_{CA}[CA]$$
$$[CA][OP] = K_1[PCA] = K_1K_2[G]$$
$$[OP][H^+] = K_B[OPH^+]$$
$$[G^-][H^+] = K_{A,G}[G]$$
$$[G][H^+] = K_{B,G}[GH^+]$$

Furthermore

$$[OP] + [OPH^+] + [PCA] + [G] + [G^-] + [GH^+] = p.$$

These equations lead to:

$$[OP]\{1 + K_{CA}[CA]/K_B[CA^-] + [CA](1 + K_2 + K_{A,G}[CA^-]/K_{CA}[CA] + K_{CA}[CA]/[CA^-]K_{B,G})/K_1K_2\} = p: \quad (1)$$

whence, if $dp/dt = -k_1[G]$,

$$\text{then } -p\ dt/dp = \{K_1K_2 + K_{A,G}[CA^-]/K_{CA}\}/[CA]k_1 + (1 + K_2)/k_1 + K_1K_2K_{CA}/k_1K_B[CA^-] + [CA]K_{CA}/[CA^-]K_{B,G}k_1. \quad (2)$$

Provided that $[GH^+]$ is negligible in the absence of added acid, a plot of reciprocal rate against 1/[CA] would yield an intercept due to the second and third terms of equation (2) and a slope due to the first bracket; both slope and intercept would vary with sodium ethoxide concentration should the concentration $[G^-]$ and $[OPH^+]$ be significantly high.

On the other hand, should the concentration of the ionic species $[OPH^+]$, $[G^-]$, and $[GH^+]$ all be low compared with p, the equation reduces to:

$$-p\ dt/dp = K_1K_2/[CA]k_1 + (1 + K_2)/k_1, \quad (3)$$

which would be applicable equally to neutral solutions (where the protonation of ethyl cyanoacetate by the oxopyrrole is not more than 12% under the experimental conditions) as well as to the alkaline solutions.

In fact, a plot of the reciprocals of the observed rates for both neutral and alkaline solutions against 1/[CA] (Fig. 3) tends to the same straight line at the higher concentrations of ethyl cyanoacetate. (In Fig. 3 [CA] refers to the total added concentration of the ethyl cyanoacetate; ionisation of the latter would, at the most, displace some points by a small amount; in Fig. 4 a correction for this ionisation has been made.) The scatter of points from the line is magnified by the reciprocal plot (in Fig. 3 the effect of a possible error of $\pm 0{\cdot}2 \times 10^{-3}$ min.$^{-1}$ in the rates is shown by vertical lines for points in neutral ethanol), and is greater than any systematic deviations at [CA] > 0·05M. At lower [CA], however, systematic deviations are manifest for both neutral and alkaline solutions and, as can be seen from the plot of reciprocal rate against cyanoacetate concentration plot (Fig. 4), their magnitude is base-dependent. Being in the direction of increased rates, these deviations cannot be accounted for by use of equation (2); however a slow side-reaction of zero order in [CA] but influenced by the pH would perhaps explain this trend. Nevertheless, that scheme (a) and equation (3) tend to predict the influence of ethyl cyanoacetate concentration upon the rate, at high concentration, is supported by the last column of Tables 1 and 2; however, these predictions are useless at [CA] < 0·05M (at which concentrations the stoicheiometry has not been established). The more

XUM

precise runs at 66° fit an equation of the same form, *viz.*, 1/Rate = 115 + 250/[CA], if an arbitrary (and experimentally unsupported) reduction of $0{\cdot}2 \times 10^{-3}$ min.$^{-1}$ is applied to the observed rates (all runs at this temperature were done at the same concentration of the oxopyrrole):

Run	65	57	66	58	61	52	49	50	53
10^3 [(obs. rate) − 0·2]	2·24	0·708	0·293	0·166	0·08	1·36	0·66	0·38	0·226
$10^3/(115 + 250/[CA])$	2·23	0·69	0·29	0·15	0·03	1·28	0·70	0·30	0·15

It should be noted that the alternative scheme of two steps at comparable rates [5] leads to a rate expression of similar form (for the aldol condensation of acetaldehyde,[8] $-3dt/da = 1/ak_1 + k_{-1}/a^2k_1k_2$) to that of equation (3). However, in the present instance scheme (b),

$$\text{Oxopyrrole} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{Intermediate} \xrightarrow{\text{CN·CH}_2\text{·CO}_2\text{Et}} \text{Products}$$

Scheme (b)

which seems *a priori* unlikely, would be required to explain the kinetic form observed at the higher ethyl cyanoacetate concentrations. A scheme based on a partly rate-determining ionisation of ethyl cyanoacetate would not only fail to account for the observed

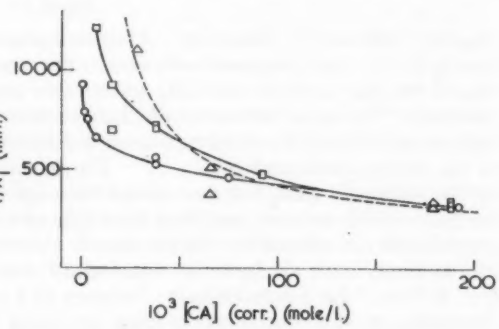


FIG. 4. *Reciprocals of the first-order rate coefficients for the reaction of ethyl cyanoacetate with 2-oxo-3,4-diphenyl-5-NNN′-trimethylguanidino-2H-pyrrole as a function of the total concentration of the former in low concentration; points are marked as in Fig.* 3.

[CA] *refers to the concentration of ethyl cyanoacetate corrected by subtraction of the concentration of sodium ethoxide. The broken curve corresponds to the line of Fig.* 3 (1/Rate = 175 + 24/[CA]).

kinetics, but would also require that the rate of ionisation be comparable (within a factor of not more than ~5) with the observed rate; however, ethyl cyanoacetate * enolises at 25° in neutral water at a rate [9] $k_1 = 7 \times 10^{-2}$ min.$^{-1}$, with an activation energy of 17 kcal. mole^{-1}.

Although equation (2) would hold for reactions in the presence of strong acid, it cannot be simply applied. Initial rates, however, are given by equation (3) when the term p is replaced by (p *minus* the concentration of added acid) (absence of hydrolysis of the acid-oxopyrrole salt being assumed); as the reaction proceeds, the guanidine so produced would tend to become protonated in proportion to its concentration and basic strength relative to those of the remaining oxopyrrole; thus an increase in specific rate during a run might be expected. Although several such runs did show deviations towards higher rates, these were not sufficiently greater than the experimental error to be significant. That the term p of equation (3) should be reduced by the amount of the protonated, and hence unavailable, oxopyrrole, is indicated when the product of the rate in neutral solution

* In ref. 4*d* the dissociation constant for diethyl malonate is misquoted (from ref. 9) as $K_a = 5 \times 10^{-4}$ (ref. 9 gives 5×10^{-14}), as is the constant for ethyl cyanoacetate as 10^{-9} (ref. 9 gives $<10^{-9}$; an empirical correlation graph given [8] does lead to 10^{-9}; the authors [9] state, however, that their graph is very rough, and is given only as a basis for argument and not for prediction—in fact, the graph leads to values of 10^{-7} for malononitrile and 10^{-10} for diethyl malonate, values quite at variance with measured values), and thus the argument on p. 2042 of ref. 4*d* is unfounded.

[8] Bell and McTigue, *J.*, 1960, 2983.
[9] Pearson and Dillon, *J. Amer. Chem. Soc.*, 1953, **75**, 2439.

XUM

and the fraction of the oxopyrrole not protonated in the acidic solution (Z; *viz.*, the predicted initial rate) is compared with the observed rate † for the latter solution:

10^5 [Acid]	0·75	1·51	3·01	4·52	6·02	7·54
$10^5 k_1$ (obs.)	3·9	3·7	2·5	1·0	0·4	0·2
Z	3·7	3·5	2·5	1·8	0·5	0·3

The elimination of the guanidine residue in the above reactions is apparently a novel aspect of guanidine chemistry (although the hydrolysis of the guanidinopyrroles [2] can be regarded as a trivial example). However, two other examples of reactions, including an elimination, of a guanidine residue in which this behaves as a " pseudo-halogen " have been observed and are under investigation in this laboratory.[10]

Comments on the Mechanism Proposed by Patai, Israeli, and Zabricky.—In a series of papers [4] Patai *et al.* propose a mechanism for the condensation of ethyl cyanoacetate, cyanoacetamide, malononitrile, and diethyl malonate with a number of aldehydes, based upon the general scheme:

$$RR'CH_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RR'CH^- + H^+ \quad . . . . . (3)$$

$$RR'CH^- + R''R'''CO \xrightarrow{k_3} RR'CH{\cdot}CR''R'''{\cdot}O^- \quad . . . . . (4)$$

Scheme (c)

step (4) is followed by fast steps. They commented " If in this sequence the dissociation rate k_1 is very slow compared with other rates, the result will be overall of the first order, *i.e.*, of the first order in $RR'CH_2$ and of zero order in the other reactants; " and they concluded " The experiments described above show that the reaction between malonitrile [*sic*] and aromatic aldehydes in water is governed by a rate-determining unimolecular ionisation of the malononitrile molecule. . . ." They comment on the difference in rates dependent on the aldehydes used, but they accept the explanation of Bird, Hughes, and Ingold [5] as adequate in this instance, and they have difficulty in explaining the faster rates, of strictly second order, in ethanol for this reaction.[4b] Yet the first-order rates for the condensation of malonitrile with aldehydes in water at 35° and apparently at pH 7 were given as *ca.* 6×10^{-5} sec.$^{-1}$ for *p*-anisaldehyde; between 12·4 and 20·7 $\times 10^{-5}$ sec.$^{-1}$ for benzaldehyde, depending on the concentration (they postulate abnormal behaviour for benzaldehyde to explain similar behaviour in its condensation with ethyl cyanoacetate in water [4c]); between 19·5 and 25·5 $\times 10^{-5}$ sec.$^{-1}$ for *p*-chlorobenzaldehyde; and between 47 and 55·5 $\times 10^{-5}$ sec.$^{-1}$ for *p*-nitrobenzaldehyde; with activation energies for these reactions which vary by a factor of four: 9300 $\pm$ 300 cal. mole^{-1} for *p*-anisaldehyde; 7200 $\pm$ 200 for benzaldehyde; and 2400 $\pm$ 300 for *p*-nitrobenzaldehyde.

For scheme (c) it can be shown, with the usual assumptions that:

$$\text{Rate}^{-1} = [H^+]k_{-1}/k_3k_1[RR'CH_2][R''R'''CO] + 1/k_1[RR'CH_2] \qquad (5)$$

(equivalent to Bird, Hughes, and Ingold's equation [5a]). If we assume that for the reaction between malononitrile and *p*-nitrobenzaldehyde the first term is negligible, then $k_1 = 55{\cdot}5 \times 10^{-5}$ sec.$^{-1}$. Then for the reaction with anisaldehyde the reciprocal of the first term will be 0·149 $\times 10^5$ and that of the second term 0·018 $\times 10^5$; with this weight the reaction would be within *ca.* 10% of second order, which was not observed. Further, the plot of the reciprocal rates for the reaction of malononitrile with benzaldehyde in water against the reciprocal of the aldehyde concentration (rates taken from ref. 4*a*) gives a plot curved downwards and hence equation (5) is not obeyed. In any case the rates and energies of activation for the ionisation of malononitrile in water are known; [9] in neutral solution at 25° in water the initial first-order rate coefficient for this reaction is 9 $\times 10^{-1}$ min.$^{-1}$ and slightly less in dilute acid; its activation energy is 18 kcal. mole^{-1}. It is thus

† Added at the suggestion of a referee.

[10] Banfield and McGuinness, unpublished work.

XUM

abundantly clear that the explanations of Patai *et al.* are inadequate, the second term in equation (5) (less than 67 sec.) being small compared with the smallest reciprocal rate (1800 sec.) and negligible compared with that for *p*-anisaldehyde (14,900 sec.).

When applying a scheme analogous to (a) and equation (2) to this reaction, it is qualitatively possible to avoid the difficulties mentioned above, and to account for the maximum in rates at *ca.* 30% ethanol in water (and of explaining similar phenomena observed for other reactions of this type [4c,d]). For a large excess of aldehyde, and on the basis of a rate-determining elimination from a species of type (G^-), the right-hand side of equation (2) would be altered by a factor of $[CA^-]K_{A,G}/[CA]K_{CA}$; however, figures given by Patai *et al.*[4a] for comparable concentrations of malononitrile and benzaldehyde (the former never being in substantial excess) are not in quantitative agreement with the appropriately modified version of equation (5); in fact the rates are reasonably described by an equation of type: $10^5k_1 = 12{\cdot}3 + a[BA]$ sec.$^{-1}$, where [BA] = the concentration of benzaldehyde; thus, on the available evidence, scheme (a) does not describe the kinetics of this reaction.

An Alternative Interpretation of Some Results of Ingold's School.[5]—These authors observed first-order rates, for a presumably unimolecular ionisation of *m*-chlorobenzhydryl chloride, which varied both with the nature of the subsequent reaction steps and with the concentration of the reagent reacting with the carbonium ion; these rates did not extrapolate to the same point at zero concentration of reagent as required by the simple theory. Their discussion of this point centred on border-line mechanisms with varying participation of the reagent. While reasonable as a qualitative explanation, this theory is unsatisfactory from a quantitative point of view (it has been criticised on theoretical grounds [11]) and, as subsequent workers have used superficially parallel behaviour to invoke the same explanation in other cases, a quantitative interpretation of these facts seems desirable.

Well-authenticated examples of this type of behaviour seem limited to ionisation in solvents of relatively low dissociating power (*e.g.*, sulphur dioxide, benzene [11,12]) in cases where the same components react in water in a conventional S_N1 manner. In the former type of solvent it might be expected that polar molecules or ion-pairs would tend to be

$$Cl^-\cdots R^+\cdots Cl^-\cdots X^+ \underset{K_2}{\overset{+X^+Cl^-}{\rightleftharpoons}} RCl \underset{K_1}{\overset{+R'_3N}{\rightleftharpoons}} RCl\cdots R'_3N \underset{K_3}{\rightleftharpoons} R^+\cdots Cl^-\cdots R'_3N \xrightarrow[k_1]{} \text{Products}$$

Scheme (d)

solvated by polar molecules in preference to solvent molecules. A scheme of form (d) leads to the rate equation, when R is the total concentration of halide present up to the rate-determining step:

$$-R\,dt/dR = (1 + K_3)/k_1 + K_1K_3/k_1[\text{Amine}] + K_1K_3[X^+Cl^-]/k_1K_2[\text{Amine}] \quad (6)$$

(where k_1 is dependent on nature of the amine); this explains qualitatively the above results and explains at least as well quantitatively the variation of the rate with amine concentration as do the linear extrapolations; [5] this may be seen from the reciprocal rate–reciprocal amine concentration plot (Fig. 5), while it retains the form of Bird, Hughes, and Ingold's equation for the effect of chloride ions on the rate. (In Fig. 5 rates are taken from ref. 5*a* for reactions of *m*-chlorobenzhydryl chloride with pyridine and triethylamine, and from ref. 5*b* for the reaction of t-butyl bromide with pyridine.) In scheme (d) the form of the complexes is not of kinetic consequence; for example, the ion quadrupole ($Cl^-\cdots R^+\cdots Cl^-\cdots X^+$) might equally be replaced by a solvated ion pair of type ($X^+Cl^-\cdots RCl$); nor is the location of the rate-determining step necessarily as shown [an alternative is the step between the complex ($RCl\cdots R^-{}_3N$) and the quadrupole; constants would be changed in the above equation, but not its form]. Thus scheme (d) seems a

[11] Gold, *J.*, 1956, 4633.
[12] Hughes, Ingold, Mok, Patai, and Pocker, *J.*, 1957, 1265.

XUM

reasonable alternative to that invoked by Ingold and his co-workers [12] to explain similar phenomena in benzene,[13] which required at least two rate-determining steps of comparable magnitude (an event which, being fortuitous, might be expected to be uncommon) in a scheme depending on competitive reactions and rearrangement of ion quadrupoles. Our scheme is fundamentally similar and it rests on similar arguments and concepts to

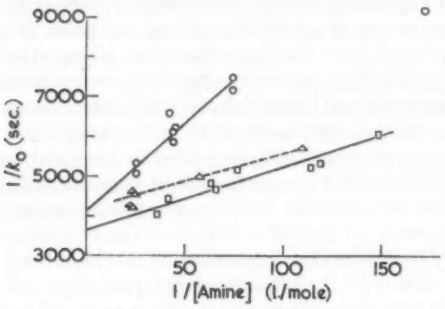


FIG. 5. *Reciprocals of the specific initial rates of the reactions of* m-*chlorobenzhydryl chloride with pyridine* (○) *and with triethylamine* (□) *and of the reaction of t-butyl bromide with pyridine* (△) *as a function of the reciprocal of the concentration of the amine, calculated from values given in the literature.*[5]

those of Ingold's school, but it differs in that one rate-determining step is replaced by a mass-significant pre-equilibrium.

However, whichever explanation proves appropriate for reactions in sulphur dioxide, it is clear that phenomena of this type—S_N1 reactions of a rate depending on the nature and/or concentration of the product-determining reagent—are to be expected only in solvents of low dielectric constant; hence care should be exercised in the parallel explanation of superficially similar behaviour, especially where the complexity of the reaction renders other explanations possible and where the phenomena are observed in aqueous solution.

UNIVERSITY OF NEW ENGLAND, ARMIDALE,
NEW SOUTH WALES, AUSTRALIA.

[*Received, December 7th*, 1960.]

[13] Hughes, Ingold, Patai, and Pocker, *J.*, 1957, 1206, 1230, 1256; Hughes, Ingold, Mok, Patai, and Pocker, *J.*, 1957, 1220; Hughes, Ingold, Mok, and Pocker, *J.*, 1957, 1238.

---

855. *Concomitant First- and Second-order Nucleophilic Substitution.*

By P. CASAPIERI and E. R. SWART.

Isotopic exchange reactions between radioactive lithium chloride and both benzyl and diphenylmethyl chloride in dimethylformamide have been studied over a range of ionic concentrations at three different temperatures. No detectable first-order contribution to the exchange was found with benzyl chloride. With diphenylmethyl chloride, however, the first- and the second-order mechanism were found to contribute equally to the overall exchange at a concentration of ~0·01M-lithium chloride. The Arrhenius activation energies for both these reactions are reported.

IN a nucleophilic exchange reaction of the type $RX + Y^- \rightleftharpoons RY + X^-$, two well-known mechanisms can occur, namely, the first-order unimolecular S_N1 and the second-order bimolecular S_N2 process. The existence of a more universal "mesomechanism" has been postulated on theoretical grounds,[1] and it is generally recognised that there is "no sharp line of demarcation" between S_N1 and S_N2 reactions.[2]

[1] Prevost, *Ind. Chim. belge*, 1958, **23**, 1231.
[2] Hughes, Ingold, and Shapiro, *J.*, 1936, 225.

The experimental evidence for the concomitant occurrence of the two mechanisms is, however, somewhat meagre and relates to systems in which the possible, or actual, occurrence of elimination, solvolysis, the mixed nature of the exchange ($X \neq Y$), or other factors complicates interpretation of the results.[2-4] Thus, although a borderline region is known to exist,[5] the actual nature of the reaction mechanism in such borderline regions is a matter of some controversy.[6]

There is, nevertheless, no reason why the overall exchange should not be regarded as the sum of unimolecular and bimolecular processes.[7] In support of this view, we now report a simple unambiguous example of simultaneous S_N1–S_N2 exchange between diphenylmethyl chloride and chloride ions ($X = Y$) in dimethylformamide, where radiochloride ions were used in the form of lithium chloride, a system in which elimination cannot occur. The system benzyl chloride–chloride ions in the same solvent was also studied and found to be overwhelmingly of S_N2 type.

The two reactions studied are both of the homogeneous form, $RX + {}^*X^- \rightleftharpoons R{}^*X + X^-$, where RX represents an organic halide and *X radioisotopically labelled halide.

In these circumstances the rate of isotopic exchange R (in mole $l.^{-1}$ $sec.^{-1}$) follows a logarithmic law regardless of mechanism, the relevant equation being [8]

$$R = -\left[\frac{ab}{t(a+b)}\right] \ln\left[1 - \frac{x}{b}\left(\frac{(a+b)}{a}\right)\right] \quad (1)$$

where a and b are the concentrations of the alkyl halide and halide salt, respectively, x is the net number of gram-ions per litre that have exchanged at time t, and x/b is given by the ratio between the activity of RX and the total radioactivity.

Le Roux and Swart [3] have shown that the constant rate of exchange R can be equated to the sum of the unimolecular and bimolecular processes (Gold [7]) by the relationship

$$R = k_1a + k_2a\alpha b, \quad (2)$$

where k_1 and k_2 are the respective rate constants for the first- and the s econd-order process, and α is the degree of ionisation of the halide salt in the solvent used. The assumption is made, in using this equation, that changes in ionic strength do not affect the rate constant k_1, at low salt concentrations. The straight-line plot of R/a against αb thus enables both k_1 and k_2 to be evaluated.

The importance of allowing for incomplete ionisation for both S_N2 and mixed S_N1–S_N2 reactions has not always been recognised and its neglect can obviously distort the results considerably. Allowance has sometimes been made for ionisation on a purely empirical basis [9] and in a few cases the actual values of α have been calculated from conductivity data.[3,10]

Part of the purpose of this paper is to show that there is no reason why the values of α should not be obtained directly from the kinetic data themselves, without assumptions as to whether a given reaction is of pure S_N2 or mixed S_N1–S_N2 type.

The value of the ionisation constant K is related to the degree of ionisation by the equation

$$K = \alpha^2f^2b/(1 - \alpha), \quad (3)$$

[3] le Roux and Swart, *J.*, 1955, 1475.
[4] Gold, Hilton, and Jefferson, *J.*, 1954, 2756; Kohnstam, Queen, and Shillaker, *Proc. Chem. Soc.*, 1959, 157.
[5] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, pp. 313 *et seq.*
[6] Grunwald, Jones, and Winstein, *J. Amer. Chem. Soc.*, 1951, **73**, 2700; Kornblum, Smiley, Blackwood, and Iffland, *ibid.*, 1955, **77**, 6299; Crunden and Hudson, *J.*, 1956, 501.
[7] Gold, *J.*, 1956, 4633.
[8] Wahl and Bonner, " Radioactivity Applied to Chemistry," John Wiley and Son, New York, 1951, p. 7.
[9] de la Mare, *J.*, 1955, 3180.
[10] Sugden, *J.*, 1949, 270; Swart and le Roux, *J.*, 1956, 2110.

where f^2 is the product of the activity coefficients for alkali and halide ions.

Combining equations (2) and (3) gives

$$\frac{(R/a - k_1)}{b} = k_2 - \frac{f^2(R/a - k_1)^2}{Kk_2b} \quad (4)$$

A plot $[(R/a) - k_1]/b$ against $f^2(R/a - k_1)^2/b$ is, therefore, a straight line of slope $1/Kk_2$ and intercept k_2.

The value of the activity coefficient f can be calculated from the standard Debye–Hückel equation

$$\log f = \frac{-1{\cdot}82 \times 10^6(\alpha c)^{\frac{1}{2}}/(\varepsilon T)^{\frac{3}{2}}}{1 + 50{\cdot}3\text{å}\ (\alpha c)^{\frac{1}{2}}/(\varepsilon T)^{\frac{1}{2}}}$$

the value of the mean distance of closest approach of the ions å (in Ångströms) being estimated from the theory of Bjerrum or of Fuoss.[11]

By successive approximation it was thus found possible to obtain the values of K, k_1, and k_2 as well as the individual values of α purely from kinetic data by using the linearity of equations (2) and (4). Clearly it is much simpler to calculate K and k_2 if k_1 is negligibly small. This in fact proved to be the case for the benzyl chloride exchange. Moreover, once K has been found for a given solvent–salt combination, from any arbitrary reaction, it can be used to obtain values of α for other reactions at other concentrations.

The values of K obtained in this way, by using Bjerrum's equation, are recorded in Table 1, the corresponding value of the mean distance of closest approach of the ions å being 1·87 Å.

These values are not significantly altered if the Fuoss equation is used instead of

TABLE 1.

Ionisation constants K for lithium chloride in dimethylformamide from kinetic data.

Temp. (K)	303·2°	313·2°	323·2°
K	0·0171	0·0156	0·0142

TABLE 2.

Rate constants k_2 (l. mole^{-1} sec.$^{-1}$) for the benzyl chloride–lithium chloride exchange in dimethylformamide.

Temp. (K)	10^3a	10^3b	$10^3R/ab$	α	$10^3k_2 = 10^3R/a\alpha b$	Temp. (K)	10^3a	10^3b	$10^3R/ab$	α	$10^3k_2 = 10^3R/a\alpha b$
303·2°	1·42	1·07	0·204	0·790	0·258	323·2°	1·39	1·05	1·35	0·770	1·75
303·2	1·42	0·704	0·207	0·831	0·249	323·2	1·39	0·692	1·41	0·811	1·73
303·2	1·42	0·343	0·225	0·892	0·252	323·2	1·39	0·337	1·50	0·878	1·71
303·2	1·47	0·106	0·245	0·955	0·257	323·2	1·45	0·104	1·60	0·948	1·72
				Mean	0·254 ± 0·004					Mean	1·73 ± 0·02
313·2	1·40	1·06	0·536	0·780	0·687						
313·2	1·40	0·698	0·556	0·821	0·677						
313·2	1·40	0·340	0·606	0·885	0·685						
313·2	1·46	0·105	0·667	0·951	0·701						
				Mean	0·688 ± 0·010						

Bjerrum's. The necessary values for the dielectric constant ε of dimethylformamide were obtained from the data of Leader and Gormley [12] by using a plot of log ε against T.

The corresponding kinetic results for benzyl chloride are recorded in Table 2.

The increase in the apparent second-order rate constant R/ab with decrease in concentration can be wholly accounted for by an increase in the degree of ionisation. The rate constants for the reaction are unexpectedly high, being some 80 times greater than the rate for the same reaction in acetone.[13]

[11] Bjerrum, *Kgl. Danske Videnskab. Selskab*, 1926, **7**, No. 9; Fuoss, *J. Amer. Chem. Soc.*, 1958, **80**, 5059.

[12] Leader and Gormley, *J. Amer. Chem. Soc.*, 1951, **73**, 5731.

[13] de la Mare and Hughes, *J.*, 1956, 845.

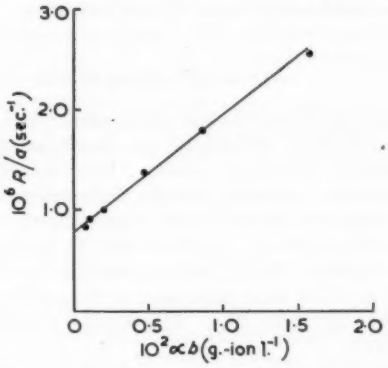
The results for the diphenylmethyl chloride–chloride ion exchange are recorded in Table 3, the values of α used being obtained from the benzyl chloride exchange.

TABLE 3.

Kinetic data for the diphenylmethyl chloride–lithium chloride exchange in dimethylformamide.

Temp. (K)	10^3a	$10^3\alpha b$	$10^4R/a$	$10^4R/a\alpha b$	Temp. (K)	10^3a	$10^3\alpha b$	$16^6R/a$	$10^4R/a\alpha b$
303·2°	5·42	1·67	0·272	0·163	323·2°	5·34	1·59	2·53	1·59
303·2	5·42	0·916	0·188	0·205	323·2	5·34	0·876	1·77	2·02
303·2	5·42	0·499	0·132	0·265	323·2	5·34	0·478	1·35	2·82
303·2	5·42	0·215	0·085	0·395	323·2	5·34	0·209	1·00	4·79
303·2	5·96	0·092	0·073	0·793	323·2	5·86	0·110	0·923	8·39
313·2	5·38	1·63	0·842	0·517	323·2	5·86	0·091	0·830	9·12
313·2	5·38	0·895	0·606	0·677					
313·2	5·38	0·488	0·431	0·883					
313·2	5·38	0·212	0·292	1·38					
313·2	5·91	0·092	0·261	2·84					

In this case the value of $R/a\alpha b$ increases continuously with decrease in ionic concentration, showing that the reaction is not purely of the second order. Plots of



Exchange between diphenylmethyl chloride and chloride ion in dimethylformamide at 50°.

R/a against αb according to equation (2), however, give good straight lines from which both k_1 and k_2 can be evaluated. An example of such a plot, namely, that at 50° C, is shown in the accompanying Figure. The rate constants thus obtained are shown in Table 4.

TABLE 4.

First- and second-order rate constants for the diphenylmethyl chloride–lithium chloride exchange in dimethylformamide.

Temp. (K)	303·2°	313·2°	323·2°
10^7k_1 (sec.$^{-1}$)	0·631 ± 0·016	2·30 ± 0·06	7·76 ± 0·19
10^5k_2 (l. mole^{-1} sec.$^{-1}$)	1·28 ± 0·03	3·86 ± 0·10	11·2 ± 0·3

These results are a clear-cut example of the simultaneous occurrence of the S_N1 and the S_N2 mechanism both contributing equally to the overall exchange at a concentration of about 0·01M-lithium chloride.

The absence of solvolysis was confirmed for both benzyl chloride and diphenylmethyl chloride by allowing these reactions to proceed to completion (12 times the half-time of exchange). Both reactions gave within <1% the theoretical maximum exchange. Moreover, there was no trend in the measured rates of exchange for the diphenylmethyl chloride reaction with time, the value of R at 50° C (for $a = 5{\cdot}34 \times 10^{-2}$; $b = 2{\cdot}31 \times 10^{-2}$ mole l.$^{-1}$) being 1·34, 1·37, 1·32, and $1{\cdot}34 \times 10^{-7}$ mole l.$^{-1}$ sec.$^{-1}$ at 1, 6, 21·5, and 45 hr., respectively.

The Arrhenius activation energies and frequency factors were determined for both reactions, with the results recorded in Table 5.

TABLE 5.

Arrhenius activation energies and frequency factors.

	E_1 (kcal. mole^{-1})	$\text{Log}_{10} A_1$	E_2 (kcal. mole^{-1})	$\text{Log}_{10} A_2$
$PhCH_2Cl$	—	—	18·6	10·8
Ph_2CHCl	24·4	10·4	21·1	10·3

The activation energy E_2 for the S_N2 process shows the expected increase in going from benzyl to diphenylmethyl chloride, due to the greater energy necessary to invert the molecule in the Walden inversion.

Ingold and his co-workers have shown [14] that changes in ionic strength can affect the rate constant k_1 for unimolecular nucleophilic substitution, particularly in solvents of low dielectric constant, according to the equation

$$k_1^{(\mu)} = k_1^{(0)} \text{ antilog}_{10} (0{\cdot}912 \times 10^{16}\ \sigma\mu/\varepsilon^2T^2)$$

where $k_1^{(0)}$ is the rate constant at zero ionic strength, $k_1^{(\mu)}$ is the rate constant at ionic strength μ, and σ is the ionic strength constant.

The presence of this effect would alter equation (2) to the form

$$R/a = k_1^{(0)} \text{ antilog } (0{\cdot}912 \times 10^{16}\sigma\alpha b/\varepsilon^2T^2) + k_2\alpha b. \qquad (5)$$

Under the conditions of dielectric constant and salt concentration chosen by us, the value of antilog $(0{\cdot}912 \times 10^{16}\sigma\alpha b/\varepsilon^2T^2)$ is close to unity and it is therefore impossible to evaluate the parameter σ from our results. However, it has been shown,[14] both on theoretical and on experimental grounds, that for diphenylmethyl halides σ is of the order of 2 Å.

Recalculation of our results, according to equation (5) with this value of σ, does not alter the values of $k_1 = k_1^{(0)}$ for the S_N1 mechanism as recorded in Table 4; nor does it alter the values of the activation energies for either the S_N1 or the S_N2 process as recorded in Table 5. The only parameter to be affected is k_2 and the values recorded in Table 4 are lowered by about 2%. This change is of the same order of magnitude as the experimental error.

In view, therefore, of the negligible change involved, we feel that the effect of ionic strength on the rate constant k_1 may legitimately be ignored for the diphenylmethyl chloride–chloride ion exchange in dimethylformamide at salt concentrations less than 0·02M.

In order to check the values of the degree of ionisation obtained from the kinetic measurements, the conductivity of lithium chloride in dimethylformamide was measured at a series of concentrations at 30° C. The results obtained were then used to calculate ionisation constants by Shedlovsky's method.[15] No value for the viscosity of dimethylformamide at 30° could be found in the literature and this was accordingly measured by means of an Ostwald viscometer and found to be 7·49 centipoises.

The value of the ionisation constant obtained in this way was 0·0178, which is in excellent agreement with the value (0·0171) obtained from the kinetic data. For comparison the values of the degrees of ionisation obtained by these two methods are recorded in Table 6.

It is interesting that simple extrapolation of the kinetic data for benzyl chloride gives values of α in fair agreement with those obtained by the more rigid procedure involving equations (2) and (4). The latter procedure is, however, the more reliable, especially if the α values are small and/or the reaction considered is to be of mixed S_N1–S_N2 type.

[14] Bateman, Church, Hughes, Ingold, and Taher, *J.*, 1940, 979; Bateman, Hughes, and Ingold, *ibid.*, p. 1017.

[15] See Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, 3rd edn., p. 288.

XUM

TABLE 6.

The degree of ionisation of lithium chloride in dimethylformamide at 30°.

10^2b	2·099	1·044	0·5222	0·2611	0·1305	0·0653	
Λ	51·08	59·37	66·81	73·04	76·78	81·06	$\Lambda_0 = 87·20$
α (condy.)	0·725	0·801	0·865	0·917	0·940	0·975	
α (kinetic)	0·720	0·795	0·855	0·908	0·945	0·978	

EXPERIMENTAL

Dimethylformamide.—Commercial dimethylformamide was dried (Na_2SO_4) and fractionated three times through a 20″ column packed with Fenske helices. Only the middle fraction was collected for use; it had d_4^{25} 0·9442, n_D^{25} 1·4290 (lit., 1·4294), b. p. 62°/25 mm.

Benzyl Chloride.—Commercial benzyl chloride was dried (K_2CO_3) and twice fractionated through the same 20″ column; it had b. p. 171·5—172°/643 mm.

Diphenylmethyl Chloride.—The commercial chloride was dried (Na_2SO_4) and fractionated three times; it had b. p. 167°/17 mm., n_D^{20} 1·5960 (lit., 1·5959), m. p. 17·0° (lit., 17—18°), Cl (Stepanov's method) 17·3% (theor. 17·5%).

Lithium Radio-chloride.—2N-[^{36}Cl]Hydrochloric acid supplied by the Radiochemical Centre, Amersham, was neutralised with pure lithium carbonate (potentiometric titration). Inactive lithium chloride was then added until the required specific activity was obtained. The solution was evaporated to dryness and the resultant active lithium chloride baked at 200° overnight (argentometric assay, 99%).

Solutions.—Solutions of both the organic halides and the lithium chloride were prepared by weighing of the respective samples and dilution to the required volume.

^{36}Cl-Labelled Organic Chlorides.—These were prepared by keeping mixtures of the chlorides with lithium chloride in dimethylformamide for prolonged periods (in excess of 2 days) at 50° (thermostat). The labelled organic halide was separated by pouring the mixtures into water and then drying the organic chloride (K_2CO_3).

Kinetic Measurements.—The reactions were carried out in H-shaped reaction vessels essentially as done by le Roux and Sugden.[16] After the reaction had proceeded for the required time, 10 ml. of the mixture were shaken with benzene (10 ml.) and water (100 ml.) in order to quench the reaction. The benzene layer was then washed with further portions of water (2 × 25 ml.).

The activities of the benzene solution and of 10 ml. of the reaction mixture in dimethylformamide were then measured consecutively in the same Geiger–Müller counter tube. When corrected, the ratio of the activity of the benzene solution to that of the reaction mixture itself gives the value of the ratio x/b in equation (1).

The correction factor by which x/b had to be multiplied was determined experimentally. Radioactive alkyl chloride, prepared as above, was dissolved in dimethylformamide to give the requisite molarity. It was then extracted with benzene in the way described for the reaction mixtures. The required correction factor F was then given by:

$$F = \frac{\text{Activity of alkyl chloride in dimethylformamide}}{\text{Activity of alkyl chloride in benzene}}$$

The value of this factor depends on the molarity of the alkyl chloride, its partition coefficient between benzene and water–dimethylformamide mixtures, and the relative β-ray absorption of benzene and dimethylformamide. The values obtained were found to be independent of the lithium chloride concentration in the range 0·02—0·2M. For 0·05M-diphenylmethyl chloride $F = 0·908$ and for 0·015M-benzyl chloride $F = 0·940$.

All concentrations were corrected for change in temperature and, where necessary, count rates were corrected for the dead time of the counting apparatus.

One of us (P. C.) is indebted to Lever Brothers (Rhodesia) (Pvt.) Limited for a Research Fellowship and we gratefully acknowledge a gift of apparatus from the Shell Company of Rhodesia Limited. We also acknowledge our debt to Dr. V. Gold (King's College, London) for helpful discussion and advice.

DEPARTMENT OF CHEMISTRY,
UNIVERSITY COLLEGE OF RHODESIA AND NYASALAND,
SALISBURY, SOUTHERN RHODESIA.

[*Received, December 16th*, 1960.]

[16] le Roux and Sugden, *J.*, 1939, 1279; 1945, 586.

856. *Organophosphorus Compounds. Part III.* Reactions of the Alkali Derivatives of Dialkyl Phosphites.*

By Zvi Pelchowicz, Sarah Brukson, and Ernst D. Bergmann.

A sodium dialkyl phosphite reacts with the dialkyl hydrogen phosphite to give the sodium alkyl hydrogen phosphite and the dialkyl alkylphosphonate.

Dimethyl phosphite, under the same conditions, gave sodium methyl methylphosphonate and disodium dimethylpyrophosphonate.

Phosphonic acids are often prepared by reaction of an alkali-metal dialkyl phosphite with an alkyl halide, the salts of diethyl and dibutyl phosphite having the advantage of being soluble in organic solvents.[1] A closer study of this reaction has shown that preparation of sodium dibutyl phosphite by reaction of dibutyl phosphite with metallic sodium is followed by a homogeneous disproportionation reaction between the sodium salt and the free phosphite ester:

$$(BuO)_2P(O)Na + (BuO)_2P(O)H \longrightarrow (BuO)_2P(O)Bu + (BuO)(NaO)P(O)H$$

Dibutyl butylphosphonate and sodium butyl hydrogen phosphite are formed. This secondary reaction proceeds at a significant rate above 60°; it lowers the yield of the dibutyl alkylphosphonates in the usual alkylation reaction and causes the alkylation products (dibutyl alkylphosphonates) to be contaminated, almost always, by dibutyl butylphosphonate.

Conditions have been found under which this reaction of a sodium dialkyl phosphite with the dialkyl hydrogen phosphite can be used for preparative purposes. Sodium alkyl hydrogen phosphites have been described by Nylén,[2] but the methods were tedious and the purity of the products was questionable. In fact, the present method shows that dialkyl phosphites can be used as alkylating agents in the same way as alkyl halides or sulphates.

Similar reactions have been observed by Petrov and his co-workers [3] and earlier by Hoffmann and Weiss [4] and by Kamai and Kukhtin; [5] trimethyl thiophosphite has also been reported to have methylating properties.[6]

Our method has given good results with diethyl, dipropyl, and dibutyl phosphite; separation of the products was easy. The dialkyl alkylphosphonates were identified by conversion into alkylphosphonyl dichlorides.[7] The sodium alkyl hydrogen phosphites were identified by analysis and infrared spectrum: the P–H,[8] P=O, and P–O–C frequencies were found at 2380, 1200—1220, and 980—1020 cm.$^{-1}$, respectively. The alkylphosphonyl dichlorides showed the P=O absorption at 1250—1300 cm.$^{-1}$; Corbridge [8] found that if the P=O bond participates in a hydrogen bridge, as in the above salts, which are partly associated, the frequency is somewhat lowered.

An unexpected reaction was observed when dimethyl phosphite was treated analogously. When an attempt was made to isolate its sodium salt (by evaporation of the methanol in which it had been prepared), an exothermic reaction set in, accompanied by evolution of dimethyl ether, and a solid mixture of salts remained which we did not succeed in resolving. It was converted in 50% yield into methylphosphonyl dichloride by successive acidification

* Part II, *J.*, 1961, 241.

[1] Kosolapoff, *J. Amer. Chem. Soc.*, 1945, **67**, 1180.
[2] Nylén, *Svensk Kem. Tidskr.*, 1936, **48**, 2.
[3] Petrov, Bliznyuk, Korshanov, Maklayev, and Voronkov, *Zhur. obshchei Khim.*, 1959, **29**, 3407.
[4] Hoffmann and Weiss, *J. Amer. Chem. Soc.*, 1956, **79**, 4759.
[5] Kamai and Kukhtin, *Zhur. obshchei Khim.*, 1957, **27**, 949.
[6] Hilgetag and Teichmann, *J. prakt. Chem.*, 1959, **8**, 73, 90.
[7] Pelchowicz, *J.*, 1961, 238.
[8] Corbridge, *J. Appl. Chem.*, 1956, **6**, 456.

XUM

with alcoholic hydrogen chloride and treatment with phosphorus pentachloride. Thus, the above exothermic reaction must have been of the Arbuzov–Michaelis type, leading to the formation of a Me–P bond. The three possible products of this reaction which would be convertible into methylphosphonyl dichloride are methyl sodium methylphosphonate, Me·PO(OMe)(ONa), disodium methylphosphonate, Me·PO(ONa)$_2$ and disodium dimethylpyrophosphonate, Me·PO(ONa)·O·PMeO(ONa);[9] only formation of the latter would explain the occurrence of dimethyl ether as a by-product. From the amount of dimethyl ether formed, it can be concluded that about 50% of the solid salt mixture consisted of disodium dimethylpyrophosphonate. Also, in the infrared spectrum of the salt mixture obtained from dimethyl phosphite and its sodium salt, the bands (900, 725 cm.$^{-1}$) characteristic of the P–O–P bond[10] have been observed.

Experimental

The following dialkyl hydrogen phosphites were prepared as described in the literature:[11–14] dimethyl, b. p. 69—73°/25 mm., 80%; diethyl, b. p. 82—86°/28 mm., 72%; dipropyl, b. p. 105—106°/15 mm., 86%. Dibutyl phosphite was a commercial product, b. p. 96—99°/2 mm.

For the preparation of the sodium salts, the appropriate sodium alkoxide is preferable to metallic sodium. For example, a solution of sodium (23 g.) in butanol (500 ml.) was cooled with ice–salt, and dibutyl phosphite (194 g.) added slowly with stirring. The excess of butanol was removed at 20 mm.; the sodium salt remained as colourless crystals (216 g.). In all cases yields were quantitative.

Reaction of Dibutyl Hydrogen Phosphite with its Sodium Salt.—Dibutyl hydrogen phosphite (194 g.) was added with stirring to a boiling solution of sodium dibutyl phosphite (216 g.) in toluene (400 ml.); heating was continued for a further 3 hr., then the toluene (from which a white precipitate had separated) was decanted and replaced by ether. The insoluble *sodium butyl hydrogen phosphite* (143 g., 90%) melted at 180—181° after recrystallisation from ethanol–acetone (Found: C, 29·7; H, 5·6. $C_4H_{10}NaO_3P$ requires C, 30·0; H, 6·3%). From the ethereal solution, dibutyl butylphosphonate (217 g., 87%), b. p. 102—120°/2 mm., was obtained by distillation.

For identification, the second product (125 g.) was added to phosphorus pentachloride (250 g.), and the mixture refluxed for 1 hr. Volatile material (butyl chloride and phosphorus oxychloride) was then removed, and the product distilled. Butylphosphonyl dichloride (49 g., 56%) had b. p. 102—103°/24 mm. (lit.,[15] 96—98°/15—16 mm., $d_4^{20\cdot5}$ 1·245, $n_D^{20\cdot5}$ 1·4655, $[M]_R$ 38·88 (calc., 37·99) (Found: C, 27·8; H, 4·8. $C_4H_9Cl_2OP$ requires C, 27·5; H, 5·2%).

Reaction of Dipropyl Hydrogen Phosphite with its Sodium Salt.—In the same way sodium dipropyl phosphite (188 g.) in benzene (200 ml.) and dipropyl hydrogen phosphite (166 g.) gave *sodium propyl hydrogen phosphite* (135 g., 92%), m. p. 196—197° (from acetone–ethanol) (Found: C, 24·5; H, 5·2. Calc. for $C_3H_8NaO_3P$: C, 24·7; H, 5·5%), and dipropyl propylphosphonate (176 g., 84%), b. p. 113—132°/24 mm. From the latter compound (104 g.) and phosphorus pentachloride (300 g.), propylphosphonyl dichloride (55 g., 68%), b. p. 90—91°/28 mm.,[16] 63—64·5°/10 mm., n_D^{27} 1·4540, d_4^{21} 1·298, $[M_R]$ 33·58 (calc., 33·37), was obtained (Found: C, 22·3; H, 3·5. Calc. for $C_3H_7Cl_2OP$: C, 22·4; H, 4·4%).

Reaction of Diethyl Hydrogen Phosphite with its Sodium Salt.—Sodium diethyl phosphite (160 g.) in toluene (100 ml.) with diethyl hydrogen phosphite (138 g.) gave *sodium ethyl hydrogen phosphite* (125 g., 94%), m. p. 182° (from ethanol–acetone) (Found: C, 18·0; H, 4·5. $C_2H_6NaO_3P$ requires C, 18·2; H, 4·6%), and diethyl ethylphosphonate (127 g., 77%), b. p. 89—97°/25 mm. The latter product (83 g.) with phosphorus pentachloride (250 g.) gave ethylphosphonyl dichloride (51 g., 70%), b. p. 74·5—75°/25 mm. (lit.,[17] 34°/3 mm.), d_4^{22} 1·368,

[9] Pelchowicz, unpublished results.
[10] (*a*) Bergmann, Littauer, and Pinchas, *J.*, 1952, 847; (*b*) Harvey and Mayhood, *Canad. J. Chem.*, 1955, **33**, 1552.
[11] Nylén, *Ber.*, 1924, **57**, 1023.
[12] Arbuzov and Vinogradova, *Bull. Acad. Sci. U.S.S.R., Classe Sci. chim.*, 1947, 617 (*Chem. Abs.*, 1948, **42**, 5844).
[13] McCombie, Saunders, and Stacey, *J.*, 1945, 380.
[14] Ramaswami and Kirch, *J. Amer. Chem. Soc.*, 1953, **75**, 1763.
[15] Razumov, Mukhacheva, and Markovich, *Zhur. obshchei Khim.*, 1958, **28**, 194.
[16] Kabachniksh and Godovikov, *Doklady Akad. Nauk U.S.S.R.*, 1956, **110**, 217.
[17] Kinnear and Perren, *J.*, 1952, 3437.

n_D^{22} 1·4495, [M_R] 28·83 (calc., 28·75) (Found: C, 16·0; H, 3·6. Calc. for $C_2H_5Cl_2OP$: C, 16·3; H, 3·4%).

Self-decomposition of Sodium Dimethyl Phosphite.—At −20°, dimethyl hydrogen phosphite (110 g.) was added to a solution of sodium (23 g.) in anhydrous methanol (400 ml.). Then the excess of methanol was removed *in vacuo* at ≯50°, a lively exothermic reaction setting in and a gas being liberated which was condensed at −78°. The reaction was moderated by cooling; when it had subsided, the product was slowly heated to 150°. Thus a white, water-soluble salt was obtained. The infrared spectrum (in a potassium bromide pellet) showed bands at 2940, 2410, 1310 1200b, 1080b, 1000, 900, 780, and 725 cm.$^{-1}$. The following assignments are made: 900 and 725, P–O–P;[10] 1000, P–O stretching in quinquevalent phosphorus compounds;[18] 1080, superposition of P–OH deformation and P=O in ionic compounds;[18] 1310 Me·P=O.[10b]

The low-temperature condensate was saturated with gaseous boron trifluoride, with cooling; the boron trifluoride complex, b. p. 127°, of dimethyl ether was obtained (lit.,[19] b. p. 127°). From 1 mole of dimethyl hydrogen phosphite, 10·7 g. of dimethyl ether have been obtained, corresponding to a 46·5% yield of disodium dimethylpyrophosphonate in the solid product.

The solid product was treated with an excess of methanolic hydrochloric acid, and the filtered solution concentrated *in vacuo*. The residual viscous oil was identified by adding it slowly to phosphorus pentachloride (400 g.); when the exothermic reaction had ceased, the product was refluxed for 2 hr., and volatile material (up to 108°) was removed. The residue (66 g., 50%) boiled at 163°, melted at 32°, and was identified as methylphosphonyl dichloride (lit.,[17] b. p. 162°, m. p. 33°).

Department of Organic Chemistry, The Hebrew University,
Jerusalem, Israel. [*Received, December 22nd*, 1960.]

[18] Bellamy and Beecher, *J.*, 1952, 1701; 1953, 728.
[19] Beilstein's "Handbuch," Vol. I, p. 282; cf. McLaughlin and Tamres, *J. Amer. Chem. Soc.*, 1960, **82**, 5618.

---

857. *A Synthesis of* 1-*Ethyl*-1,2,3,5-*tetrahydro*-10-*methyl*-7,8-*methylenedioxy*-5-*oxobenzo*[f]*pyrrocoline, a Degradation Product of Lycorine.*

By Shuzo Takagi and Shojiro Uyeo.

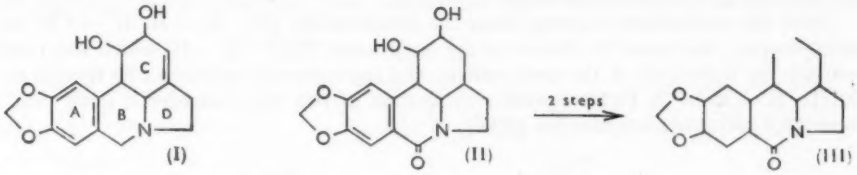
The structure of the compound (III), a degradation product of the alkaloid lycorine with the same number of carbon atoms as the natural product, has been established by synthesis of its racemate, providing further proof of the structure of the alkaloid.

Previously [1] we have shown that dihydrolycorinone (II) derived from the alkaloid, lycorine (I), undergoes oxidative scission of ring c with lead tetra-acetate or periodic acid to give a dialdehyde, which was smoothly converted through its bis(ethylene dithioacetal) into the derivative (III). We now record a synthesis of the racemate of compound (III), providing yet another proof of the structure of the alkaloid lycorine and its congeners.

Treatment of isosafrol (IV) with iodine and mercuric oxide according to Bougault's procedure [2] gave α-(3,4-methylenedioxyphenyl)propionaldehyde (V) which was characterised as its oxime and 2,4-dinitrophenylhydrazone. A Strecker reaction converted this aldehyde into 1-cyano-2-(3,4-methylenedioxyphenyl)propylamine (VI; R = H, R′ = CN) which with formic acid under reflux suffered partial hydrolysis of the cyano-group along with formylation of the amino-group to give 1-carbamoyl-*N*-formyl-2-(3,4-methylenedioxyphenyl)propylamine (VI; R = CHO, R′ = CO·NH_2); presence of

[1] Takagi, Taylor, Uyeo, and Yajima, *J.*, 1955, 4003.
[2] Bougault, *Bull. Soc. chim. France*, 1901, **25**, 856.

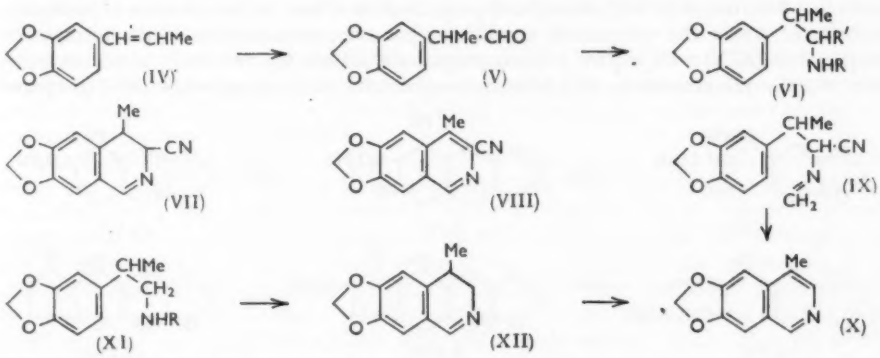
the amide group * was confirmed by its infrared spectrum which showed two strong carbonyl bands at 1661 and 1629 cm.$^{-1}$ but no CN band.



In our initial attempts to set up the A/B ring system of (III), we cyclised the amide (VI; R = CHO, R′ = CO·NH_2) with phosphorus oxychloride by the Bischler–Napieralski reaction. The product thus obtained in 30% yield was 3-cyano-3,4-dihydro-4-methyl-6,7-methylenedioxyisoquinoline (VII) which exhibited a CN band at 2217 cm.$^{-1}$ but no carbonyl absorption in the infrared spectrum. When the reaction was carried out in a xylene solution, however, a different compound, $C_{12}H_8N_2O_2$, containing two hydrogen atoms less than (VII), was the only isolable basic product. The ultraviolet spectrum of this compound exhibited bands which were quite different from those of (VII) and resembled those of isoquinoline (Fig. 1), and structure (VIII) was therefore assigned to it. The ready elimination of two hydrogen atoms by aerial oxidation from the obvious intermediate (VII) must be due, at least in part, to the electron-attracting effect of the cyano-group.

We next attempted to obtain 3-cyano-1,2,3,4-tetrahydro-4-methyl-6,7-methylenedioxyisoquinoline from the azomethine (IX) under the Pictet–Spengler conditions. The only product isolated in a crystalline form was, however, not the expected compound. It had the formula, $C_{11}H_9NO_2$, which was confirmed by the analytical values of the picrate and the ultraviolet spectrum of the base was comparable to that of (VIII) (Fig. 1), indicating that the compound was, not a tetrahydroisoquinoline, but an isoquinoline. The structure (X), indicated by these findings, was proved by the following unambiguous synthesis.

Reduction of the oxime of α-(3,4-methylenedioxyphenyl)propionaldehyde (V) with lithium aluminium hydride yielded the amine (XI; R = H) which with formic acid gave



the formamide (XI; R = CHO). Bischler–Napieralski cyclisation of this furnished the 3,4-dihydroisoquinoline (XII) which on dehydrogenation with palladium–charcoal in cymene gave compound (X), identical with the sample obtained as above. How the isoquinoline (X) was formed under Pictet–Spengler conditions is not clear, but elimination

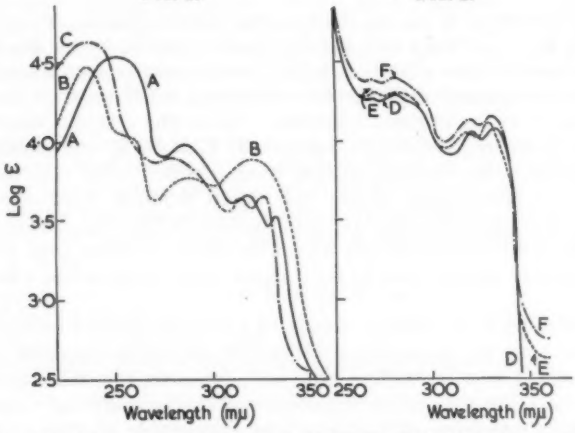
* We are very grateful to a Referee for suggesting this possibility.

XUM

of the elements of hydrogen cyanide from the first formed 3-cyano-1,2,3,4-tetrahydro-4-methyl-6,7-methylenedioxyisoquinoline could occur, followed by an aerial oxidation of the resulting 1,2-dihydroisoquinoline.

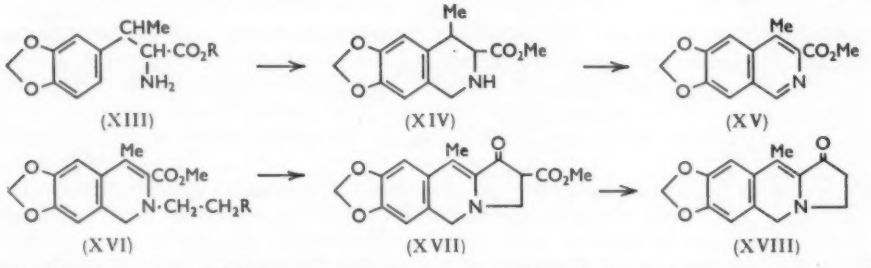
Since the cyclisations starting from the amino-nitrile (VI; R = H, R′ = CN) were unsatisfactory, we turned to the use of the amino-acid (XIII; R = H) which was readily available by hydrolysis of the amino-nitrile and conveniently isolated as its methyl ester (XIII; R = Me). A Pictet–Spengler cyclisation of this ester afforded a good yield of the 1,2,3,4-tetrahydroisoquinoline (XIV).

FIG. 1. FIG. 2.



FIGS. 1 and 2. *Absorption spectra of compounds* (A) VIII, (B) VII, (C) X, (D) XVI, R = CN, (F) XVIII, *and* (E) *oxime of* XVIII.

In order to build up ring C it was next desired to alkylate the nitrogen atom of the isoquinoline (XIV) with a β-halogenopropionate or a β-halogenopropionitrile. Leonard, Swann, and Fuller[3] have reported successful reaction of ethyl 1,2,3,4-tetrahydroisoquinoline-3-carboxylate with ethyl β-iodopropionate in xylene in the presence of potassium carbonate: under the comparable conditions, however, condensation of the tetrahydroisoquinoline (XIV) with methyl β-bromopropionate did not proceed well; also unsatisfactory was the quaternisation, with β-bromopropionitrile, of the isoquinoline (XV) [prepared

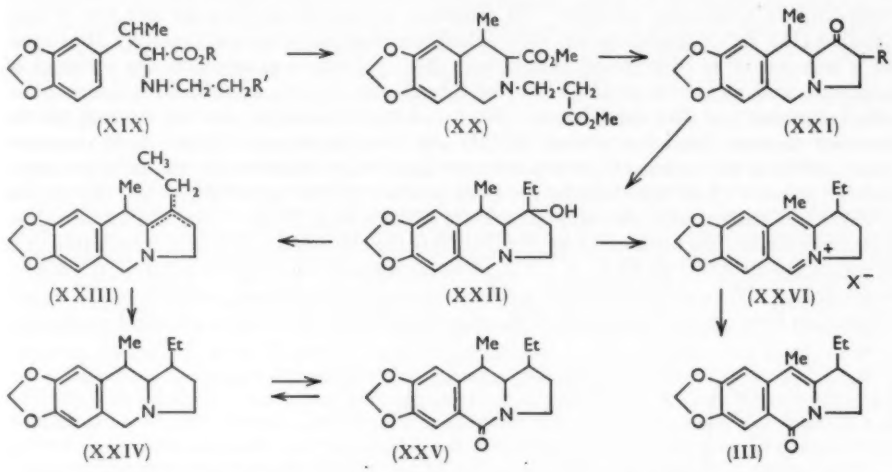


by boiling the ester (XIV) in xylene in the presence of palladium–charcoal and cinnamic acid].

We then tried to cyanoethylate the secondary amine (XIV), but the reaction proceeded neither in acetic acid nor in an alkaline solution with Triton B as condensing agent. On

[3] Leonard, Swann, and Fuller, *J. Amer. Chem. Soc.*, 1954, **76**, 3193.

the other hand, the base (XIV) with 2-bromoethyl cyanide in the presence of potassium carbonate gave a low yield of a cyanoethyl derivative which was isolated as the picrate, $C_{16}H_{16}N_2O_4,C_6H_3N_3O_7$. The free base, regenerated from this picrate, was soluble in



benzene and its ultraviolet spectrum indicated the presence of a double bond conjugated with the methylenedioxybenzene ring (Fig. 2); structure (XVI; R = CN) was therefore assigned to it. Hydrolysis of the cyano-group and simultaneous esterification with methanol and hydrochloric acid then afforded the diester (XVI; R = CO_2Me) which was cyclised by metallic potassium in xylene under the Dieckmann conditions. The resulting crude keto-ester (XVII) was saponified and decarboxylated in boiling hydrochloric acid to ketone (XVIII). As expected, the ultraviolet spectrum of this ketone resembled that of the nitrile (XVI; R = CN) (Fig. 2); its infrared spectrum exhibited a broad band at 3250 cm.$^{-1}$ (OH) but no bands were detected in the carbonyl region, suggesting that the keto-group exists under the conditions of the measurement entirely in the enol form although formation of an oxime leaves no doubt about the presence of a reactive carbonyl group in this compound. Although this ketone (XVIII) might have been expected to lead to the desired benzo[*f*]pyrrocoline (III) in four steps, the extremely low overall yield precluded its use. The following approach, which in essence reverses the order of some of the above steps, was more profitable.

Although the amino-nitrile (VI; R = H, R′ = CN) did not react with acrylonitrile under the conditions reported by McKinney and Uhuig,[4] the corresponding ester (XIII; R = Me) gave a good yield of compound (XIX; R = H, R′ = CN). Hydrolysis and esterification with methanolic hydrochloric acid, followed by treatment with formaldehyde and hydrochloric acid at pH 4 under the conditions of Pictet–Spengler cyclisation, then afforded the tetrahydroisoquinoline (XX), and Dieckmann ring closure was accomplished by the use of sodium hydride. The resulting keto-ester (XXI; R = CO_2Me) was decarboxylated in boiling hydrochloric acid, yielding the ketone (XXI; R = H) which exhibited in the infrared spectrum a carbonyl band at 1754 cm.$^{-1}$ characteristic of a five-membered cyclic ketone, in agreement with its expected structure.

With ethylmagnesium bromide in tetrahydrofuran this ketone gave the alcohol (XXII) which with boiling acetic anhydride gave an *O*-acetate rather than an olefin (XXIII). The acetate reverted to the tertiary alcohol (XXII) on hydrolysis in ethanolic sodium

[4] McKinney and Uhuig, *J. Amer. Chem. Soc.*, 1950, **72**, 2599.

hydroxide. By the use of phosphorus oxychloride in pyridine, however, the alcohol (XXII) gave the olefin (XXIII) which was hydrogenated to give the saturated compound (XXIV) (stereochemistry not established). Oxidation of this by potassium permanganate furnished the oily lactam (XXV): the lactam reverted to crystalline (XXIV) on reduction with lithium aluminium hydride. All attempts to convert the lactam into the desired product (III) by dehydrogenation with palladium–charcoal were unsuccessful: thus most of it was recovered after being heated with 30% palladium–charcoal in the presence of cinnamic acid in xylene at 160—170° for 2 hours, in cymene at 200° for 3 hours, or in ethyl cinnamate at 250° for 5 hours. We had noticed, however, that on working up the reaction mixture from the alcohol (XXII) and phosphorus oxychloride there remained unextracted in the aqueous layer a quaternary base which could be isolated as its sparingly soluble picrate. This base became the main product (yields up to 85%) when the alcohol (XXII) was treated with an excess of thionyl chloride in pyridine. The analytical values of the picrate and the ultraviolet spectra (Fig. 3) of the chloride derived from it indicated that it must have structure (XXVI; X = Cl), probably formed as a result of a shift of the double bond in (XXIII) accompanied by aerial oxidation of the resulting 1,4-dihydroisoquinoline. Potassium ferricyanide then oxidised the chloride (XXVI; X = Cl) to a neutral compound,

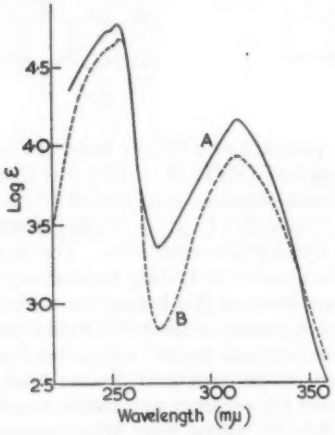


FIG. 3. *Absorption spectra of* (A) 4-*methyl*-6,7-*methylenedioxyisoquinoline methiodide and* (B) *compound* XXVI (X = Cl).

$C_{16}H_{17}NO_3$, m. p. 150°, which was shown to be the racemate of the degradation product (III) of lycorine by comparison of the infrared spectra in chloroform and the ultraviolet spectra in ethanol.

Preliminary attempts, so far without success, to resolve the amide (III) have centred on crystallisation of suitable quaternary salts (XXVI).

The synthesis of this compound provides an unambiguous proof of the structure of lycorine (I), since this was derived from the alkaloid, without loss of carbon atoms, under conditions that precluded molecular rearrangements.

EXPERIMENTAL

α-(3,4-*Methylenedioxyphenyl*)*propionaldehyde* (V).—Iodine (64 g.) was added to a stirred mixture of isosafrole (40 g.), yellow mercuric oxide (60 g.), and a small amount of iodine in ether saturated with water, in small portions during 30 min., with cooling in ice. Additional mercuric oxide (10 g.) was added, and stirring was continued at 13—15° for about 4 hr., until the colour of iodine disappeared. Mercuric salts were filtered off, and a solution of sodium hydrogen sulphite (70 g.) and potassium iodide (8 g.) in water (120 ml.) was added to the filtrate, which was stirred until precipitation of the bisulphite addition compound of the

aldehyde was complete. The adduct, m. p. 175°, was dissolved in water, basified with aqueous sodium carbonate, and extracted with benzene. Drying (Na_2SO_4) and evaporation of the benzene extract and distillation of the residue gave α-(3,4-*methylenedioxyphenyl*)*propionaldehyde* (33·8 g.), b. p. 95—95·5°/0·32 mm. (Found: C, 67·3; H, 5·8. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·7%). The 2,4-*dinitrophenylhydrazone* formed orange prisms (from ethyl acetate), m. p. 140° (Found: C, 53·6; H, 4·0; N, 15·4. $C_{16}H_{14}N_4O_6$ requires C, 53·6; H, 3·9; N, 15·6%). The *oxime* was prepared in the usual manner and formed prisms (from ethanol), m. p. 72° (Found: C, 62·0; H, 5·7; N, 7·1. $C_{10}H_{11}NO_3$ requires C, 62·2; H, 5·7; N, 7·3%).

1-*Cyano*-2-(3,4-*methylenedioxyphenyl*)*propylamine* (VI; R = H, R′ = CN).—To a solution of the aldehyde (V) (10 g.) in ethanol (20 ml.) was added, with stirring, 50% sodium cyanide solution (10 ml.), 27% aqueous ammonia (20 ml.), and ammonium chloride (5 g.), the temperature rising and the mixture separating into two layers. More water was added, when necessary, until ammonium chloride passed completely into the aqueous layer. The mixture was heated with frequent shaking in a sealed vessel at 50—60° for 10 hr., then cooled, diluted with water, and extracted with benzene. The benzene layer was washed with water and extracted with 10% hydrochloric acid which immediately began to deposit crystals of the *hydrochloride* (cf. VI; R = H, R′ = CN) (10·2 g.). Recrystallisation from ethanol gave needles, m. p. 187—188° (decomp.) (Found: C, 54·8; H, 5·4; N, 11·5. $C_{11}H_{12}N_2O_2$,HCl requires C, 54·9; H, 5·4; N, 11·6%). This gave the free *base* as needles, m. p. 88° (from ethanol) (Found: C, 64·4; H, 5·8; N, 13·5. $C_{11}H_{12}N_2O_2$ requires C, 64·7; H, 5·9; N, 13·7%).

1-*Carbamoyl*-N-*formyl*-2-(3,4-*methylenedioxyphenyl*)*propylamine* (VI; R = CHO, R′ = $CO{\cdot}NH_2$).—1-Cyano-2-(3,4-methylenedioxyphenyl)propylamine (VI; R = H, R′ = CN) (1·4 g.) was heated with 85% formic acid (9 ml.) at 180° for 2 hr. After cooling, the mixture was poured on ice, then set aside at 0° overnight, and the precipitate was collected. Crystallisation from acetone gave the *diamide* (VI; R = CHO, R′ = $CO{\cdot}NH_2$) as scales (1·3 g.), m. p. 219—220° (decomp.) (Found: C, 57·4; H, 5·7. $C_{12}H_{14}N_2O_4$ requires C, 57·6; H, 5·6%).

3-*Cyano*-3,4-*dihydro*-4-*methyl*-6,7-*methylenedioxyisoquinoline* (VII).—The diamide (VI; R = CHO, R′ = $CO{\cdot}NH_2$) (0·3 g.) was heated in phosphorus oxychloride (5 ml.) on a water bath until evolution of hydrogen chloride ceased. The mixture was evaporated under reduced pressure and the residue taken up in water (10 ml.), filtered, and washed with benzene. The aqueous layer was basified with aqueous sodium hydroxide and extracted with benzene. The extracts were washed with water, dried, and concentrated to give a residue which was chromatographed in benzene on alumina (7 g.). Elution with benzene gave the *dihydroisoquinoline* (VII) (83 mg.), needles (from benzene), m. p. 177—178° (Found: C, 67·0; H, 4·8; N, 13·1. $C_{12}H_{10}N_2O_2$ requires C, 67·3; H, 4·7; N, 13·1%).

3-*Cyano*-4-*methyl*-6,7-*methylenedioxyisoquinoline* (VIII).—The diamide (VI; R = CHO, R′ = $CO{\cdot}NH_2$) (0·3 g.) and phosphorus oxychloride (1·5 ml.) in dry xylene (10 ml.) were heated on a water bath for 30 min. After cooling, the mixture was extracted with 5% hydrochloric acid (50 ml.) which was basified and extracted with chloroform. The chloroform extract was washed with water, dried, and evaporated to give a residue (0·16 g.) which was chromatographed in chloroform on alumina (2 g.). The chloroform eluate gave the *base* (VIII) (40 mg.) which crystallised from benzene as needles, m. p. 173—175° (Found: C, 67·5; H, 3·8. $C_{12}H_8N_2O_2$ requires C, 67·9; H, 3·8%).

4-*Methyl*-6,7-*methylenedioxyisoquinoline* (X).—(*a*; cf. below) Addition of 37% formaldehyde solution (0·3 ml.) to an aqueous solution (5 ml.) of the hydrochloride (0·3 g.) of the amino-nitrile (VI; R = H, R′ = CN) in water (5 ml.) caused immediate precipitation of the azomethine (IX) which formed scales (from acetone), m. p. 222—223° (decomp.). A solution of the azomethine (0·3 g.) in methanol (50 ml.) was adjusted to pH 4·0 with hydrochloric acid; 37% aqueous formaldehyde (0·5 ml.) was then added, and the whole was kept at 30° for 64 hr. The mixture was neutralised with aqueous sodium hydroxide and evaporated, and the residue was dissolved in 10% hydrochloric acid (10 ml.) and washed with chloroform. The aqueous layer was basified with 20% aqueous sodium hydroxide (10 ml.) and extracted with chloroform which was washed with water, dried, and evaporated. Chromatography of the residue (0·24 g.) in chloroform over alumina (2 g.) and elution with chloroform gave the *compound* (X) (60 mg.), needles (from ether), m. p. 113—114° (Found: C, 70·4; H, 4·7. $C_{11}H_9NO_2$ requires C, 70·6; H, 4·9%). The *picrate* formed needles (from methanol), m. p. 235° (decomp.) (Found: C, 49·0; H, 2·7. $C_{17}H_{12}N_4O_9$ requires C, 49·0; H, 2·8%).

2-(3,4-*Methylenedioxyphenyl*)*propylamine* (XI; R = H).—The oxime (9 g.) of the aldehyde

(V) in ether (50 ml.) was refluxed with lithium aluminium hydride (2·7 g.) for 5 hr. After cooling, the excess of reagent was destroyed by water, and the ethereal layer extracted with 5% hydrochloric acid. The acid extract was basified with aqueous ammonia and extracted with ether. This second ether solution was dried and evaporated to dryness, to give the amine (XI; R = H) as an oil (7·8 g.). The *hydrogen oxalate* had m. p. 177—178° (from ethanol) (Found: C, 53·4; H, 5·6; N, 5·1. $C_{10}H_{13}NO_2,C_2H_2O_4$ requires C, 53·5; H, 5·6; N, 5·2%). The *N*-formyl derivative (XI; R = CHO) was prepared by heating the amine (6 g.) with 85% formic acid (3 ml.) at 170—190° for 2 hr. and distilled under reduced pressure as an oil (4·8 g.), $\nu_{max.}$ 1685 cm.$^{-1}$ (film).

3,4-*Dihydro*-4-*methyl*-6,7-*methylenedioxyisoquinoline* (XII).—The preceding *N*-formyl derivative (4·6 g.) and phosphorus oxychloride (14 g.) were refluxed in xylene (20 ml.) for 40 min. Addition of light petroleum (b. p. 30—60°) caused separation of a brown oil which was taken up in water, washed with ether, basified with aqueous sodium hydroxide, and extracted with chloroform. The chloroform extract was dried and evaporated and the residue distilled under reduced pressure, to give the dihydroisoquinoline (XII) as an oil (1·4 g.). The *picrate* formed needles (from methanol), m. p. 181—182° (Found: C, 48·9; H, 3·4; N, 13·3. $C_{11}H_{11}NO_2,C_6H_3N_3O_7$ requires C, 48·8; H, 3·4; N, 13·4%).

4-*Methyl*-6,7-*methylenedioxyisoquinoline* (X).—(*b*; cf. above) The dihydroisoquinoline (XII) (0·2 g.), regenerated from its picrate, was heated in *p*-cymene (5 ml.) in the presence of 30% palladium–charcoal (0·3 g.) under nitrogen at 200° for 1 hr. After being kept at room temperature overnight, the catalyst and crystals which separated were collected and extracted with chloroform which was then shaken with 5% hydrochloric acid. The *p*-cymene layer was also extracted with 5% hydrochloric acid. The combined aqueous layers were basified with aqueous ammonia and extracted with ether which was dried and evaporated. The residue was passed in chloroform through a column of alumina. Evaporation of the chloroform eluate and crystallisation from benzene gave the isoquinoline (X) as needles (50 mg.), m. p. 116—118° (Found: C, 70·5; H, 4·7; N, 7·6%). The picrate formed yellow needles (from methanol), m. p. 235—237° (decomp.) (Found: C, 49·1; H, 2·9; N, 13·6%). This base and its picrate showed no depression of m. p.s on admixture with respective preparations described above. The infrared and ultraviolet spectra were also identical. The methiodide was prepared in the usual manner and crystallised from acetone: it had m. p. 267—268° (decomp.).

Methyl α-*Amino*-β-(3,4-*methylenedioxyphenyl*)*butyrate* (XIII; R = Me).—1-Cyano-2-(3,4-methylenedioxyphenyl)propylamine hydrochloride (10 g.) in methanol (100 ml.) was saturated with dry hydrogen chloride and refluxed on a water bath for 20 hr. The methanol was evaporated under reduced pressure and the residue taken up in water (100 ml.). This solution was filtered, basified with sodium carbonate, and extracted with ether. The ethereal extract was dried and evaporated and the residue (6·1 g.) distilled at 154—158°/0·27 mm., giving the oily ester (XIII; R = Me). The ester, in ether, gave its *hydrochloride*, deliquescent needles, m. p. 175° (from ethanol–ether) (Found: C, 53·1; H, 5·2; N, 4·8. $C_{12}H_{15}NO_4$,HCl requires C, 52·8; H, 5·5; N, 5·1%). The *picrate* formed yellow needles (from methanol), m. p. 178° (decomp.) (Found: C, 46·3; H, 3·7; N, 11·8. $C_{12}H_{15}NO_4,C_6H_3N_3O_7$ requires C, 46·4; H, 3·9; N, 12·0%).

Methyl 1,2,3,4-*Tetrahydro*-4-*methyl*-6,7-*methylenedioxyisoquinoline*-3-*carboxylate* (XIV).—A solution of the butyrate (XIII; R = Me) (1·3 g.) in 10% hydrochloric acid (10 ml.) was adjusted to pH 3·5 with aqueous sodium hydroxide. 37% Aqueous formaldehyde (2 ml.) was then added to the solution and the whole kept at 30° for 30 hr. After addition of 35% hydrochloric acid (1 ml.), the mixture was heated on a water bath for 30 min., filtered from some resin, washed with ether, and basified with sodium carbonate, and the precipitated solid was collected, washed with water, and dried, to give the *tetrahydroisoquinoline* (XIV) (1·1 g.). This crystallised from methanol as needles, m. p. 171—172° (Found: C, 62·9; H, 5·8. $C_{13}H_{15}NO_4$ requires C, 62·6; H, 6·1%). The *hydrochloride*, m. p. 247° (decomp.) (Found: C, 54·3; H, 5·5. $C_{13}H_{15}NO_4$,HCl requires C, 54·6; H, 5·6%), and the *picrate*, m. p. 226° (decomp.) (Found: C, 47·7; H, 3·6; N, 11·8. $C_{13}H_{15}NO_4,C_6H_3N_3O_7$ requires C, 47·7; H, 3·8; N, 11·7%), both crystallised as needles from methanol.

Methyl 4-*Methyl*-6,7-*methylenedioxyisoquinoline*-3-*carboxylate* (XV).—The tetrahydroisoquinoline (XIV) (0·3 g.), cinnamic acid (0·36 g.), and 30% palladium–charcoal (0·2 g.) in xylene (20 ml.) were heated in a current of carbon dioxide at 160—170° for 2 hr. The mixture was filtered and the filtrate extracted with 5% hydrochloric acid. The acidic extracts were washed with ether, basified with sodium carbonate, and extracted with benzene. The benzene extracts

XUM

were washed with water, dried, and evaporated, to give a residue (0·21 g.) which on crystallisation from methanol gave the *isoquinoline* (XV) as needles, m. p. 183° (Found: C, 63·5; H, 4·4; N, 5·7; OMe, 12·5. $C_{13}H_{11}NO_4$ requires C, 63·7; H, 4·5; N, 5·7; OMe, 12·7%).

Methyl 2-*Cyanoethyl*-1,2-*dihydro*-4-*methyl*-6,7-*methylenedioxyisoquinoline*-3-*carboxylate* (XVI; R = CN).—The tetrahydroisoquinoline (XIV) (0·34 g.), 2-bromoethyl cyanide (0·25 g.), and anhydrous potassium carbonate (0·25 g.) were heated with occasional stirring on the water bath for 8 hr., then cooled. Water (20 ml.) was added, and the mixture was extracted with benzene which was washed with water, dried, and evaporated to dryness. The residue (0·19 g.) distilled at 160—175° (bath temp.)/0·8 mm. The distillate (0·1 g.) was converted into its *picrate*, needles (from methanol), m. p. 274° (decomp.) (Found: C, 49·7; H, 3·2; N, 13·1. $C_{16}H_{16}N_2O_4,C_6H_3N_3O_7$ requires C, 49·9; H, 3·6; N, 13·2%). The free base (XVI; R = CN) was regenerated by passing a chloroform solution of the picrate through alumina, and crystallised from ether as needles, m. p. 87—90°.

1,2,3,5-*Tetrahydro*-10-*methyl*-7,8-*methylenedioxy*-1-*oxobenzo*[f]*pyrrocoline* (XVIII).—The distillate (0·4 g.) consisting of (XVI; R = CN) in methanol (30 ml.) was saturated with dry hydrogen chloride and refluxed with constant bubbling of dry hydrogen chloride at a slow rate through the mixture for 6 hr. The methanol was then evaporated under reduced pressure and the residue taken up in water (50 ml.). This solution was filtered, basified with sodium carbonate, and extracted with benzene. The benzene extract was dried and evaporated, and the residue (0·22 g.) distilled at 128—132°/0·3 mm., giving the diester (XVI; R = CO_2Me) as a pale yellow, viscous oil (0·2 g.). This (0·2 g.) was added in dry toluene (2 ml.) to a suspension of powdered potassium (0·15 g.) in toluene (5 ml.), and the whole was heated on a water bath with occasional shaking for 2 hr. After cooling, the excess of the potassium was destroyed with ethanol, then concentrated hydrochloric acid (15 ml.) was added to the mixture and the whole heated on the water bath for 3 hr. After evaporation to dryness under reduced pressure, the residue was taken up in water (50 ml.), basified with sodium carbonate, and extracted with benzene. The extracts were washed with water, dried, and evaporated to dryness, to give a residue which was distilled at 180—220° (bath temp.)/0·6 mm. Crystallisation of the distillate (20 mg.) from ether yielded the *pyrrocoline* (XVIII) as needles, m. p. 91—92° (Found: C, 68·8; H, 5·9; N, 6·2. $C_{14}H_{13}NO_3$ requires C, 69·1; H, 5·4; N, 5·8%). The *oxime* formed needles (from water), m. p. 85—90°, which was raised to m. p. 99—100° by drying in a vacuum over phosphorus pentoxide (Found, after drying: N, 8·8. $C_{14}H_{14}N_2O_3,3H_2O$ requires N, 9·0%).

α-(2-*Cyanoethylamino*)-β-(3,4-*methylenedioxyphenyl*)*butyric Acid* (XIX; R = H, R′ = CN).—Methyl α-amino-β-(3,4-methylenedioxyphenyl)butyrate (4·2 g.) and sodium hydroxide (0·66 g.) in water (10 ml.) were stirred at room temperature for 30 min. Acryolnitrile (0·91 g.) was then added with cooling and the whole stirred for a further 3 hr. After being kept overnight at 0°, the mixture was heated at 50° for 1 hr., then cooled, washed with ether, and acidified with 35% hydrochloric acid (1·4 ml.). The precipitate was collected, washed with water and ether, and dried, to give the *butyric acid* (XIX; R = H, R′ = CN) (3·5 g.). Crystallisation from water gave needles, m. p. 191—192°, soluble in acids and alkaline solutions and giving a positive ninhydrin test (Found: C, 57·7; H, 6·1; N, 9·8. $C_{14}H_{16}N_2O_4,H_2O$ requires C, 57·1; H, 6·2; N, 9·5%).

Methyl α-(2-*Methoxycarbonylethylamino*)-β-(3,4-*methylenedioxyphenyl*)*butyrate* (XIX; R = Me, R′ = CO_2Me).—The butyric acid (XIX; R = H, R′ = CN) (6 g.) in methanol (70 ml.) was saturated with dry hydrogen chloride. After being refluxed for 10 hr., the mixture was evaporated and the residue taken up in water (100 ml.), filtered, washed with ether, basified with sodium carbonate, and extracted with ether. The ethereal extracts were dried and evaporated to dryness, to give a residue (3·1 g.) which was distilled at 145—165° (bath temp.)/0·05 mm., yielding the *ester* (XIX; R = Me, R′ = CO_2Me) as a viscous oil (Found: C, 59·3; H, 6·6; OMe, 19·2. $C_{16}H_{21}NO_6$ requires C, 59·4; H, 6·6; 2OMe, 19·2%).

Methyl β-(1,2,3,4-*Tetrahydro*-3-*methoxycarbonyl*-4-*methyl*-6,7-*methylenedioxy*-2-*isoquinolyl*)-*propionate* (XX).—A solution of the ester (XIX; R = Me, R′ = CO_2Me) (4·4 g.) in water (30 ml.) containing 35% hydrochloric acid (1 ml.) was adjusted to pH 4·0 with aqueous sodium hydroxide. 37% Aqueous formaldehyde (13 ml.) was then added and the whole kept at 32° for 4 days. After addition of 35% hydrochloric acid (1 ml.), the mixture was heated on a water bath for 30 min., filtered from resin, washed with ether, basified with sodium carbonate, and extracted with ether. The ethereal extracts were combined, washed with water, dried, and evaporated to dryness, to give a residue (3·2 g.) which was chromatographed in benzene

over alumina. Elution with benzene gave a pale yellow oil (XX) which resisted crystallisation. The hydrochloride was very deliquescent. The *picrolonate* prepared in the usual manner formed yellow needles, m. p. 180—181°, from acetone–ether (Found: C, 54·2; H, 4·9; N, 11·5; OMe, 10·5. $C_{17}H_{21}NO_6$,$C_{10}H_8N_4O_5$ requires C, 54·1; H, 4·9; N, 11·7; 2OMe, 10·4%).

1,2,3,5,10,10a-*Hexahydro*-10-*methyl*-7,8-*methylenedioxy*-1-*oxobenzo*[f]*pyrrocoline* (XXI; R = H).—To a stirred suspension of sodium hydride (1 g.) in dry toluene (20 ml.) was added a solution of the ester (XX) (7·2 g.) in dry toluene (20 ml.) in two portions at 90°, the second portion being added dropwise after evolution of hydrogen had been observed. After addition of a few drops of ethanol, the mixture was heated at that temperature with stirring for 4 hr. The excess of the sodium hydride was destroyed with ethanol, concentrated hydrochloric acid (270 ml.) added, and the whole boiled under reflux with stirring for 3 hr., a negative ferric chloride test being then obtained. The mixture was evaporated to dryness, diluted with water (200 ml.), and filtered from resin, and the filtrate basified with sodium carbonate and extracted with ether. The extracts were combined, washed with water, dried, and evaporated to give a residue (5·7 g.). Two crystallisations of this residue from methanol gave the *ketone* (XXI; R = H) as yellow needles (3·9 g.), m. p. 150—151° (decomp.). It gave a positive Zimmermann test (Found: C, 68·3; H, 6·1; N, 6·1. $C_{14}H_{15}NO_3$ requires C, 68·6; H, 6·2; N, 5·7%). The *oxime* was prepared in methanol and formed prisms (from methanol), m. p. 216—217° (decomp.) (Found: C, 64·5; H, 6·2; N, 10·4. $C_{14}H_{16}N_2O_3$ requires C, 64·6; H, 6·2; N, 10·8%).

1-*Ethyl*-1,2,3,5,10,10a-*hexahydro*-1-*hydroxy*-10-*methyl*-7,8-*methylenedioxybenzo*[f]*pyrrocoline* (XXII).—To a Grignard solution prepared from magnesium (1·5 g.) and ethyl bromide (4·2 g.) in tetrahydrofuran (20 ml.) was added with stirring the ketone (XXI; R = H) (3 g.) in tetrahydrofuran (80 ml.). Stirring was continued under reflux for 4 hr. The solvent was then removed and the residue decomposed with ice-water and hydrochloric acid and filtered. The filtrate was made alkaline with aqueous ammonia and extracted with chloroform. This extract was washed with water, dried, and evaporated, to give a residue (2·5 g.) which was chromatographed in benzene (12 ml.) over alumina (25 g.). Benzene and chloroform eluates gave the *alcohol* (XXII) as scales, m. p. 149—150° (from methanol) (Found: C, 69·5; H, 7·6; N, 5·0. $C_{16}H_{21}NO_3$ requires C, 69·8; H, 7·7; N, 5·1%). The O-*acetate* was prepared by treatment of the alcohol (XXII) (0·4 g.) with acetic anhydride at 150° for 1 hr. and formed needles, m. p. 125°, from methanol (Found: C, 67·8; H, 7·4. $C_{18}H_{23}NO_4$ requires C, 68·1; H, 7·3%).

1-*Ethyl*-2,3-*dihydro*-10-*methyl*-7,8-*methylenedioxy*-3H-*benzo*[f]*pyrrocolinium Salts* (XXVI).—(i) To a solution of the alcohol (XXII) (0·7 g.) in dry pyridine (6 ml.) was added, with cooling in ice-water, phosphorus oxychloride (0·4 ml.), and the mixture was heated on a water bath for 40 min. After being kept at room temperature overnight, the mixture was added to ice-water and evaporated to dryness. The residue was dissolved in water (50 ml.), basified with aqueous ammonia, and extracted with ether. Evaporation gave the olefin (XXIII) as an oil (0·19 g.). The alkaline aqueous layer was weakly acidified with hydrochloric acid and filtered, and a saturated sodium picrate solution was added. The picrate thus formed was collected, washed with ether, and passed in acetone (40 ml.) through alumina (5 g.). Elution with acetone and crystallisation from acetone gave the *picrate* (cf. XXVI) as yellow needles (0·34 g.), m. p. 175—176° (decomp.) (Found: C, 54·6; H, 4·1; N, 11·4. $C_{16}H_{15}NO_2$,$C_6H_3N_3O_7$ requires C, 54·5; H, 4·2; N, 11·6%). The hydrochloride was prepared by passage of the picrate in methanol through a column of Amberlite IRA 400 ion-exchange resin (OH^- form), followed by acidification with hydrochloric acid and concentration. Crystallisation from acetone–methanol gave hygroscopic needles, m. p. 184—186°.

(ii) To a stirred solution of the alcohol (XXII) (0·32 g.) in dry pyridine (6·3 ml.) was added thionyl chloride (0·5 ml.) with cooling. Stirring was continued for 10 min. and then the mixture was left at room temperature for 2 hr. After evaporation under reduced pressure, a solution of the residue in water (50 ml.) was filtered, basified with aqueous ammonia, and extracted with ether. Concentration of the ethereal extract gave the olefin (XXIII) as an oil (15 mg.). The aqueous layer was treated with sodium picrate as described in (i), yielding the picrate (cf. XXVI) (0·48 g.), m. p. and mixed m. p. 173—175°.

Attempts to resolve the base by the use of (+)-tartaric acid, (−)-dibenzoyltartaric acid, (+)-camphoric acid, (−)-quinic acid, or (+)-di-*p*-toluoyltartaric acid failed.

1-*Ethyl*-1,2,3,5,10,10a-*hexahydro*-10-*methyl*-7,8-*methylenedioxybenzo*[f]*pyrrocoline* (XXIV).—A solution of the olefin (XXIII) (0·5 g.) in acetic acid (25 ml.) was shaken with hydrogen in the

presence of Adams catalyst (90 mg.) (uptake 71 ml. in 40 min.). The mixture was filtered, and the combined filtrate and washings were evaporated under reduced pressure. The residue was taken up in water, basified with aqueous ammonia, and extracted with ether. The ethereal extract was washed with water, dried, and concentrated, to give a residue (485 mg.) which was chromatographed in benzene–light petroleum (b. p. 30—60°) (1 : 1) over alumina (2 g.). Elution with benzene–light petroleum (b. p. 30—60°) (1 : 1) gave the *pyrrocoline* (XXIV) (330 mg.) which crystallised from light petroleum as plates, m. p. 92—95° (Found: C, 73·9; H, 8·1. $C_{16}H_{21}NO_3$ requires C, 74·1; H, 8·2%).

1-*Ethyl*-1,2,3,5,10,10a-*hexahydro*-10-*methyl*-7,8-*methylenedioxy*-5-*oxobenzo*[f]*pyrrocoline* (XXV).—To a solution of the base (XXIV) (66 mg.) in acetone (12 ml.) was added with stirring a 1% solution of potassium permanganate in acetone (7·2 ml.) at 1—2°. Stirring was continued for a further 3 hr. and the mixture kept at room temperature overnight. After removal of manganese dioxide, the filtrate was evaporated to dryness and the residue taken up in benzene, washed with 3% hydrochloric acid, water, and aqueous sodium hydrogen carbonate, dried, recovered (62 mg.), and distilled at 180—185° (bath temp.)/0·01 mm. The viscous distillate was the *lactam* (XXV) (55 mg.) which was analysed after one redistillation (Found: C, 70·1; H, 7·1; N, 5·0. $C_{16}H_{19}NO_3$ requires C, 70·3; H, 7·0; N, 5·1%).

The *lactam* (XXV) (60 mg.) and lithium aluminium hydride (70 mg.) in tetrahydrofuran (5 ml.) were heated under reflux for 4 hr. Working up in the usual manner gave a base which after chromatography and recrystallisation had m. p. 92°, undepressed on admixture with a sample of the base (XXIV) described above.

Attempted Dehydrogenation of the Lactam (XXV).—(i) The lactam (228 mg.), cinnamic acid (0·12 g.), and 30% palladium–charcoal (70 mg.) in xylene (15 ml.) were heated in a stream of carbon dioxide at 160—170° for 2 hr. The mixture was filtered and washed with 5% aqueous sodium hydrogen carbonate and water, dried, and evaporated, to give a residue (200 mg.) which was purified by passing through alumina. A benzene eluate gave an oil which was identical with the starting material (ultraviolet and infrared spectra; paper chromatography). (ii) Lactam (63 mg.), cinnamic acid (83 mg.), and 30% palladium–charcoal (70 mg.) in *p*-cymene (10 ml.) were heated under nitrogen at 200° for 3 hr.; starting material (36 mg.) was recovered. (iii) Dehydrogenation in ethyl cinnamate at 250° for 5 hr. and chromatography on alumina gave starting material as the main fraction, with minute amounts of two compounds, m. p. 125—127° and 215—220°, severally, whose infrared spectra were quite different from that of the lactam (III); these compounds were not investigated further.

1-*Ethyl*-1,2,3,5-*tetrahydro*-10-*methyl*-7,8-*methylenedioxy*-5-*oxobenzo*[f]*pyrrocoline* (III).—To a solution of the quaternary chloride (cf. XXVI) (54 mg.) in 50% aqueous ethanol (2 ml.) was added one of potassium ferricyanide (0·22 g.) and potassium hydroxide (40 mg.) in water (4 ml.). After being heated on a water bath for 3 hr., the mixture was neutralised with dilute sulphuric acid and evaporated to dryness. The residue was dissolved in water (30 ml.) and extracted with benzene, and the benzene extract washed with dilute sulphuric acid and water, dried, and evaporated to give a further residue (31 mg.). This was chromatographed in benzene over alumina (3 g.). Elution with benzene gave the lactam (III) which on crystallisation from benzene–light petroleum (b. p. 30—60°) formed needles, m. p. 150° (Found: C, 71·0; H, 6·4; N, 5·3. Calc. for $C_{16}H_{17}NO_3$: C, 70·8 H, 6·3; N, 5·2%). The infrared spectrum in chloroform was identical with that of a sample from natural sources. The ultraviolet spectra of the two samples were superimposable.

We are indebted to Dr. W. I. Taylor for reading the manuscript and to Dr. N. Yanaihara, Mr. M. Watatani, Mr. M. Saheki, and Miss N. Fujita for technical assistance.

School of Pharmacy, Osaka University, Japan.
[Present addresses: Mukogawa Women's University, Hyogo (S. T.).
Faculty of Pharmacy, Kyoto University, Kyoto (S. U.).] [*Received, March 13th*, 1961.]

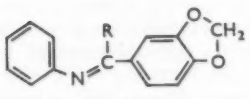
858. *An Examination of the Rutaceae of Hong Kong. Part VIII.* The Synthesis of the Alkaloid, Graveoline.*

By H. R. Arthur and (Miss) Lucy Y. S. Loh.

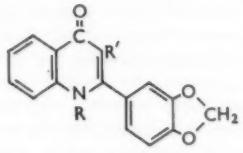
The alkaloid, graveoline [1-methyl-2-(3,4-methylenedioxyphenyl)-4-quinolone] (VI), from *Ruta graveolens* has been synthesised.

Ohta and Miyazaki [1] showed that the Japanese species of *Ruta graveolens* contained the alkaloids skimmianine and kokusaginine, and Ohta, Mori, Noda, and Aoki [2] later reported the presence of bergapten in the plant. In Part VI [3] it was reported that the Hong Kong species contained the alkaloids skimmianine and kokusaginine; this contained also a new alkaloid graveoline which was shown to be 1-methyl-2-(3,4-methylenedioxyphenyl)-4-quinolone by comparison with an authentic sample of this compound kindly sent to us by Dr. S. Goodwin who had prepared it in the course of her extensive work [4] on quinolone alkaloids but had not isolated it from a natural source.

Graveoline (VI) has now been synthesised also by us. Piperonylic acid was converted into its chloride and thence its anilide. The latter, on treatment with phosphorus pentachloride by the method of Elderfield *et al.*,[5] yielded an oily imidoyl chloride (I) which crystallised on storage at 0°. This crude product, with diethyl sodiomalonate,[5] yielded the diester (II) which was not isolated but on cyclisation afforded the pure quinolone



(I) R = Cl;
(II) R = $CH_2(CO_2Et)_2$



(V) R = R′ = H
(VI) R = Me, R′ = H

(III) R = H, R′ = CO_2Et
(IV) R = H, R′ = CO_2H

ester (III). Alkaline hydrolysis gave the corresponding acid (IV) which was smoothly decarboxylated by copper powder in quinoline at 175—180°, to give 2-(3,4-methylenedioxyphenyl)-4-quinolone (V). Finally, *N*-methylation yielded graveoline (VI).

It is interesting that heating of the acid (IV) under reduced pressure in a cold-finger apparatus gave readily a sublimate which had a m. p. similar to that of the acid (IV) and was not depressed on admixture. Attempted decarboxylation with copper powder in boiling glycerol gave a solid (m. p. >300°) which when methylated did not yield graveoline and is believed to have lost the methylenedioxy-group. When boiling quinoline and copper powder were used decarboxylation took place, as shown by the infrared absorption spectrum, but again the product did not yield graveoline. However, by the quinoline method at 170—180°, the acid (IV) gave in 10 minutes an almost quantitative yield of the product (V) and during this reaction carbon dioxide was evolved. Although the quinolone (V) did not depress the m. p. of the acid (IV) it was clearly a new and decarboxylated product, as shown by its infrared spectrum and by its conversion into graveoline on methylation. We conclude that the sublimate of the acid (IV) referred to above is actually the decarboxylated quinolone (V) and that it did not depress the m. p. of the former because the acid becomes decarboxylated to a certain extent during the m. p. determination.

* Part VII, *J.*, 1961, 3551.

[1] Ohta and Miyazaki, *J. Pharm. Soc. Japan*, 1958, **78**, 538.
[2] Ohta, Mori, Noda, and Aoki, *Chem. and Pharm. Bull.* (*Japan*), 1960, **8**, 377.
[3] Arthur and Cheung, *Austral. J. Chem.*, 1960, **13**, 510.
[4] Goodwin, Smith, and Horning, *J. Amer. Chem. Soc.*, 1957, **79**, 2239, and later papers.
[5] Elderfield, Gensler, Bembry, Kremer, Head, Brody, and Frohardt, *J. Amer. Chem. Soc.*, 1946, **68**, 1272.

XUM

Work is in progress to check this and to determine the nature of the other products obtained.

Experimental

Analyses are by Dr. K. W. Zimmermann, C.S.I.R.O. and University of Melbourne, Microanalytical Laboratory. M. P.s were taken on a gas-heated copper block except where otherwise stated. Infrared spectra were taken for Nujol mulls on a Perkin–Elmer Infracord (model 137) spectrophotometer. The alumina used for chromatography was of B.D.H. analysis grade.

N-Phenylpiperonylamide.—Piperonylic acid (10·0 g.) obtained from piperonaldehyde by the method given [6] for the disproportionation of benzaldehyde, was converted into piperonyl chloride by treatment with boiling thionyl chloride (6·0 ml.). The excess of thionyl chloride was removed and aniline (6·0 ml.) was added to the residue. The mixture was warmed on the steam-bath for ½ hr. The brown product was washed with dilute hydrochloric acid and aqueous sodium carbonate and then crystallised once from methanol and twice from benzene, giving colourless *N-phenylpiperonylamide* (15·1 g.), m. p. 144—145° (Found: C, 69·9; H, 4·6; N, 6·0. $C_{14}H_{11}NO_3$ requires C, 69·7; H, 4·6; N, 5·8%).

Ethyl 1,4-*Dihydro*-2-(3,4-*methylenedioxyphenyl*)-4-*oxoquinoline*-3-*carboxylate.*—The preceding amide (15·0 g.) was treated with phosphorus pentachloride (13·5 g.) at 110—115° for 1 hr. by the method of Elderfield *et al.*[5] for the preparation of imidoyl chlorides. Removal of phosphorus oxychloride at the pump left a yellow oil which at 0° gave crude crystalline *N*-phenylpiperonylimidoyl chloride. Sodium (1·6 g.) was dissolved in magnesium-dried ethanol (19·8 ml.). Diethyl malonate (9·9 ml.) was added. Removal of ethanol at the pump left a residue which was added in suspension in sodium-dried toluene (200 ml.) to the crude imidoyl chloride. The mixture was boiled under reflux for 3½ hr. Toluene was removed at the pump and the residue was extracted with water and ether. Distillation of the dried ethereal layer left a brown oil from which diethyl malonate was removed *in vacuo*. The brown semisolid residue was heated under reduced pressure at 150—170° for 3½ hr., then at 180—190° for ½ hr. As much as possible of the residue was taken up in cold benzene (300 ml.) and applied to a column of alumina. Elution with benzene gave *N*-phenylpiperonylamide. Elution with chloroform gave a brown oil. Elution with methanol then gave the *ester* (III) which after crystallisation from ethanol was deposited as needles or prisms, m. p. 228° (Found: C, 67·9; H, 4·9; N, 4·2. $C_{19}H_{15}NO_5$ requires C, 67·7; H, 4·5; N, 4·2%). The portion of the residue insoluble in cold benzene was shown to consist entirely of this ester (total yield, 3·4 g.).

1,4-*Dihydro*-2-(3,4-*methylenedioxyphenyl*)-4-*oxoquinoline*-3-*carboxylic Acid.*—The preceding ester (1·5 g.) was boiled under reflux with 40% aqueous-ethanolic sodium hydroxide for 7 hr. The solution, on cooling, was acidified. The *acid* (IV) was collected and crystallised from 2-methoxyethanol as needles (0·9 g.), m. p. 291—292° (Found: C, 65·6; H, 4·0; N, 4·4. $C_{17}H_{11}NO_5$ requires C, 66·0; H, 3·6; N, 4·5%).

2-(3,4-*Methlenedioxyphenyl*)-4-*quinolone.*—The acid (IV) (0·9 g.) was heated in quinoline (5 ml.) containing a little copper powder at 175—180° for 10 min., then allowed to cool. The crystalline *quinolone* (V) (0·7 g.) that separated was collected and recrystallisated three times from ethanol, forming needles, m. p. 290—291° (Found: C, 72·8; H, 4·2; N, 4·8. $C_{16}H_{11}NO_3$ requires C, 72·4; H, 4·2; N, 5·3%).

1-*Methyl*-2-(3,4-*methylenedioxyphenyl*)-4-*quinolone* [*Graveoline* (VI)].—The quinolone (V) (0·7 g.) was treated in methanol (25 ml.) at 60° alternately with potassium hydroxide and drops of methyl sulphate for 1½ hr. The methanol was distilled off and water (250 ml.) was added. Crystals separated, which on recrystallisation from ethanol formed needles, m. p. 204—205° (Kofler block), that did not depress the m. p. of graveoline; its infrared spectrum was identical with that of the natural product (Found: C, 72·4; H, 4·9; N, 5·0. Calc. for $C_{17}H_{13}NO_3$: C, 73·1; H, 4·7; N, 5·0%).

The authors thank Professor J. Miller for interest and the Research Grants Committee of the University of Hong Kong for a grant-in-aid. A grant kindly provided by the Nuffield Foundation, from which the infrared spectrophotometer was purchased, is gratefully acknowledged.

Department of Chemistry,
University of Hong Kong, Hong Kong. [*Received, March 30th,* 1961.]

[6] Cohen, "Practical Organic Chemistry," 3rd Edn., Macmillan and Co. Ltd., London, 1949, p. 236.

859. *The Hydrolysis of Acetic Anhydride. Part VII.* Catalysis by Pyridine and Methylpyridines in Acetate Buffers.*

By A. R. Butler and V. Gold.

The effect of pyridine, 2- and 3-picoline, and 2,6-lutidine on the rate of hydrolysis of acetic anhydride in acetate buffer has been measured and related to the spectrophotometrically determined concentrations of unprotonated base in solution. There is no detectable catalysis by the 2-substituted bases. The catalytic effect of pyridine is inversely proportional to the concentration of acetate ions in solution, and it is reduced by a factor of 5 ± 1 on replacement of the solvent by deuterium oxide. The results agree with a mechanism in which 1-acetylpyridinium ions are formed reversibly from pyridine and acetic anhydride, the subsequent hydrolysis of these ions being rate-determining.

The pyridine-catalysed hydrolysis of acetic anhydride in aqueous solution was studied by Gold and Jefferson [1] who formulated the mechanism as

$$Ac_2O + Py \underset{-1}{\overset{1}{\rightleftharpoons}} PyAc^+ + OAc^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$PyAc^+ + H_2O \xrightarrow[2]{} AcOH + PyH^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

the 1-acetylpyridinium ion ($PyAc^+$) being an unstable intermediate. It was then considered that reaction 1 was the rate-controlling step since (in 50% acetone–water) the catalytic coefficient of pyridine was not found to bear an inverse relation to the concentration of acetate ion.

During some recent experiments on the spontaneous and catalysed hydrolysis of acetic anhydride in deuterium oxide it was observed that the pyridine-catalysed hydrolysis was considerably retarded by the change in solvent from ordinary water to deuterium oxide.[2] This result (which is more fully reported in the present paper) prompted us to examine the kinetics of the catalysis by pyridine bases in greater detail, since it appeared improbable that reaction (1) could be subject to a large solvent isotope-effect. A similar rate-controlling transfer of an acetyl cation (from acetic anhydride to a formate ion) is thought to be the mechanism of catalysis by formate ions [3] and, as expected for such a mechanism, only a very small solvent isotope-effect is found in this case.[2,4]

The use of buffer solutions in the experiments now reported permitted observation of the catalysed hydrolyses as first-order reactions, since it ensured the constancy of the concentration of free pyridine (as distinct from protonated pyridine) during each kinetic run. This concentration was determined for each buffer mixture by spectrophotometric measurements similar to those described by Herington.[5] In this way it was possible to assess separately the effect of added acetate ion on the concentration of free pyridine and its effect on the velocity of the pyridine-catalysed hydrolysis at a given concentration of free pyridine.

Experimental

Reagents were purified as described in earlier Parts of the series, with the following exceptions:

2,6-Lutidine was warmed with urea (120 g.) and water (40 ml.) to 80° and the white

* Part VI, *J.*, 1961, 2305.

[1] Gold and Jefferson, *J.*, 1953, 1409.
[2] Butler and Gold, *Proc. Chem. Soc.*, 1960, 15.
[3] Kilpatrick, *J. Amer. Chem. Soc.*, 1928, **50**, 2891; Gold and Jefferson, *J.*, 1953, 1416.
[4] Butler and Gold, *J.*, 1961, 2305.
[5] Herington, *Discuss. Faraday Soc.*, 1950, **9**, 26; Andon, Cox, and Herington, *Trans. Faraday Soc.*, 1954, **50**, 918.

crystalline complex formed was filtered off and washed rapidly with water. Distillation of a mixture of the crystals with water (200 ml.) yielded the water–2,6-lutidine azeotrope (b. p. 96°) from which lutidine separated on addition of solid sodium hydroxide. The lutidine was dried (NaOH) and distilled. The whole procedure was repeated twice more, the final product distilling sharply at 143°. The object of this treatment was the removal of unhindered homologues or isomers since the formation of the urea complex is stated to be specific to 2,6-substituted pyridines.[6]

3-Picoline (200 g.) was freed from isomeric impurities[7] by refluxing it with phthalic anhydride (50 g.) and acetic anhydride (50 g.) for 4 hr. The mixture was poured into water (1 l.), rendered alkaline with sodium hydroxide, and distilled (b. p. of azeotrope with water, 97°). A 2-picoline layer was formed on addition of solid sodium hydroxide. It was separated, dried (NaOH), and distilled (b. p. 143°).

Hydrolysis velocities of acetic anhydride were determined in sodium acetate–acetic acid buffer solutions containing a low concentration of the pyridine base. In order to keep the extent of protonation of the bases to a minimum, the concentration of acetic acid in the buffer solutions was made as low as was compatible with the requirement of constancy of the degree of protonation during the course of a run. (In experiments with 2,6-lutidine—which was catalytically inactive—it was more important to achieve a high rather than a constant concentration of free base, and the concentration of acetic acid in the buffer was almost of the same magnitude as the concentration of acetic acid generated during the hydrolysis.) The reactions were followed by the modified[4] method of Lees and Saville.[8]

The media for kinetic experiments were prepared by diluting 10 ml. of an accurately prepared aqueous solution of a pyridine base to 250 ml. with sodium acetate–acetic acid buffer solution. The degree of protonation of the pyridine bases in these buffer media was determined spectrophotometrically as follows. Three separate aliquot portions (5 ml.) of the above solution of pyridine base in buffer solution were separately diluted to 25 ml. with (i) N-sulphuric

TABLE 1.

Specimen evaluation of α, for pyridine.

$10^5[Py]_{stoich.}$	2·74	5·76	7·76	9·31	11·72
D_{PyH^+}	0·155	0·309	0·417	0·491	0·621
D_{Py}	0·082	0·152	0·191	0·242	0·292
D	0·100	0·207	0·279	0·331	0·418

acid, (ii) N-sodium hydroxide, and (iii) a sodium acetate–acetic acid solution prepared by diluting 960 ml. of the buffer employed in preparing a reaction medium with water to 1 l. The buffer concentration in a solution resulting from dilution (iii) is the same as that in the reaction medium, so that (apart from a temperature effect discussed below) the degree of protonation of the pyridine base in this solution should also equal that in the reaction medium. Dilutions (i) and (ii) cause complete conversion of the pyridine base into the protonated and the unprotonated form, respectively. The optical densities of the diluted solutions were measured in matched 1 cm. quartz cells at a suitable wavelength (252 mμ for pyridine, 270 mμ for 2,6-lutidine, 262 mμ for 2-picoline, and 260 mμ for 3-picoline), a corresponding solution without pyridine base being used in the reference beam of the spectrophotometer. If the optical densities of the solutions resulting from dilutions (i), (ii), and (iii) are designated by the symbols D_{PyH^+}, D_{Py}, and D, respectively, the portion (α) of the pyridine base present in the unprotonated form is given by $\alpha = (D_{PyH^+} - D)/(D_{PyH^+} - D_{Py})$. This determination was repeated for several concentrations of a pyridine base, and the best value of α was evaluated from the slopes of the straight lines obtained by plotting the three optical densities against the stoicheiometric concentration of the pyridine base. The procedure is illustrated for pyridine (Table 1). The slopes of the three lines are: for D, 3590; for D_{PyH^+}, 5310; for D_{Py}, 2550 mole^{-1} l.; whence $\alpha = (5310 - 3590)/(5310 - 2550) = 0{\cdot}62_4$.

The experiments with deuterium oxide involved a scaling-down of the same general procedure.

The optical density measurements were performed with a Beckman DU spectrophotometer, without temperature regulation, and relate to a temperature of 22° ± 3°. We must consider

[6] U.S.P. 2,376,008.
[7] Riethof, Richards, Savitt, and Othmer, *Ind. Eng. Chem., Analyt. Ed.*, 1946, **18**, 458.
[8] Lees and Saville, *J.*, 1958, 2262.

whether the value of α determined at this temperature may be applied to the evaluation of catalytic coefficients at 25°. The temperature-dependence of α at a fixed acetate-buffer composition is governed by the temperature-dependence of the ratio of acid dissociation constants K_{AcOH}/K_{PyH^+}. The temperature-variation of K_{AcOH} is well-known to be very small in this region and that of the dissociation constants of pyridinium and 2-picolinium ions can be evaluated from thermochemical measurements.[9] It follows from these data that the values of α which were measured at 22° ± 3° should be increased by *ca.* 5 ± 5% in order to apply at 25°.

TABLE 2.

Pyridine catalysis.

(a) *Effect of varying pyridine concentration*: $\alpha = 0{\cdot}62_4$

$10^4[Py]_{stoich.}$ (M)	$10^4[Py]_{free}$ (M)	10^3k (sec.$^{-1}$)	$10^3(k - k_{Buffer})$ (sec.$^{-1}$)	$(k - k_{Buffer})/[Py]_{free}$ (sec.$^{-1}$ mole^{-1} l.)
0	0	2·89	—	—
1·99	1·24	3·65	0·76	6·1
2·88	1·80	4·04	1·15	6·4
3·88	2·42	4·44	1·55	6·4
4·91	3·06	4·88	1·99	6·5
6·89	4·30	5·67	2·78	6·5

(b) *Experiments in deuterium oxide*: [AcONa] = 0·015M; $\alpha = 0{\cdot}32_2$

$10^4[Py]_{stoich.}$	$10^4[Py]_{free}$	10^3k	$10^3(k - k_{Buffer})$	$[OAc^-](k - k_{Buffer})/[Py]_{free}$
0	0	$0{\cdot}97_1$	—	—
4·37	1·41	$1{\cdot}44_6$	$0{\cdot}47_5$	0·049

(c) *Effect of varying acetate concentration*:

$10^4[Py]_{stoich.}$	α	$10^4[Py]_{free}$	100[NaOAc]	10^3k	10^3k_{Buffer}	$10^3(k - k_{Buffer})$	$(k - k_{Buffer})/[Py]_{free}$
3·99	0·592	2·36	6·21	4·26	2·84	1·42	6·0
5·86	0·524	3·07	3·66	4·95	2·74	2·21	7·2
4·98	0·494	2·46	3·55	4·64	2·74	1·90	7·7
5·28	0·429	2·26	2·44	4·95	2·70	2·25	10·0
5·85	0·351	2·05	1·82	5·14	2·67	2·47	12·0
5·25	0·318	1·67	1·53	5·41	2·66	2·75	16·5

From graph in Fig. 2: $[OAc^-](k - k_{Buffer})/[Py]_{free} = 0{\cdot}25$.

TABLE 3.

Effect of other pyridine bases.

(a) 2-*Picoline*: $\alpha = 0{\cdot}23_9$ (0·23)

$10^4[Pic.]_{stoich.}$	$10^4[Pic.]_{free}$	10^3k
0	0	2·89
4·57	1·05	2·89
7·92	1·82	2·89
11·1	2·55	2·89
13·3	3·06	2·90
16·2	3·72	2·89

(b) 3-*Picoline*: $\alpha = 0{\cdot}32_4$ (0·39)

$10^4[Pic.]_{stoich.}$	$10^4[Pic.]_{free}$	10^3k	$10^3(k - k_{Buffer})$	$(k - k_{Buffer})/[Pic.]_{free}$
0	0	2·89	—	—
2·49	0·81	4·49	1·60	20
4·51	1·46	5·96	3·07	21
6·94	2·25	7·72	4·83	21
9·15	2·96	8·90	6·01	20
11·4	3·69	10·60	7·71	21

(c) 2,6-*Lutidine*: $\alpha = 0{\cdot}083$

$10^4[Lut.]_{stoich.}$	$10^4[Lut.]_{free}$	10^3k
0	0	2·89
7·88	0·65	2·89
11·5	0·96	2·88
16·2	1·35	2·89
22·6	1·88	2·88

Such a correction has not been applied in the evaluation of the quoted catalytic coefficients which are accordingly subject to a corresponding systematic error. The error is of marginal significance and, in particular, does not affect the conclusions drawn from the series of experiments with pyridine and different concentrations of acetate.

The effect on the reaction of pyridine, 2- and 3-picoline, and 2,6-lutidine was measured at different concentrations of pyridine base. The same buffer solution was used for the first

[9] Levi, McEwan, and Wolfenden, *J.*, 1949, 760.

three bases; that used with 2,6-lutidine was slightly less acidic. The apparent catalytic coefficient of each base in a given medium was evaluated from the slope of the graph (Fig. 1) of the experimental first-order rate coefficient against the concentration of free base (*i.e.*, $[Py]_{free} = \alpha[Py]_{stoich.}$). The rectilinear course of these graphs for pyridine and 3-picoline indicates first-order dependence on the catalyst concentration. All individual runs conformed accurately to the first-order law (*i.e.*, first-order in acetic anhydride).

In the case of pyridine alone, the catalysis was also studied as a function of the concentration of acetate ion. Under these conditions, acetate catalysis makes a different contribution to the reaction velocity at each concentration. The pyridine-catalysed contribution to the rate was therefore evaluated by subtracting from each measured rate constant the rate constant (k_{Buffer}) for the particular buffer medium in the absence of pyridine. These control values were calculated from the previously determined catalytic coefficient for acetate ions.[4] The apparent catalytic coefficient of pyridine $(k - k_{Buffer})/[Py]_{free}$ was plotted against the reciprocal of the concentration of acetate ions in solution (Fig. 2).

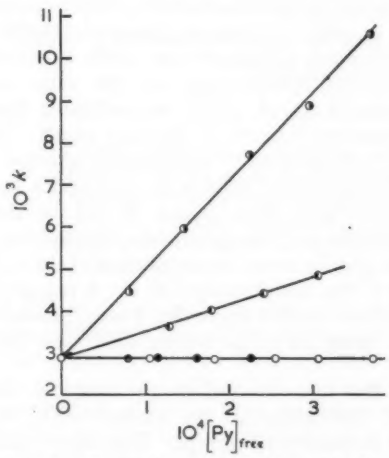


FIG. 1. Dependence of reaction velocity on catalyst concentration.

◐ Pyridine. ○ 2-Picoline. ◑ 3-Picoline. ● 2,6-Lutidine.

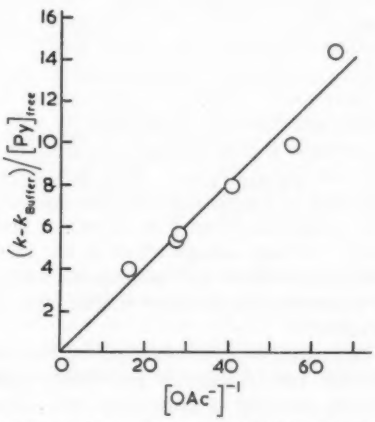


FIG. 2. Dependence of pyridine catalysis upon acetate concentration.

The earlier groups of experiments (Tables 2a and 3) were carried out before the full importance of the concentration of acetate ions in the reaction had been realised, and the buffer solutions used in these experiments were not made up exactly. However, since the first group of experiments on pyridine (Table 2a) and those on the two picolines relate to the same batch of buffer solution, the determined relative values of α should be consistent with the known dissociation constants of these bases.[5] To test this, a second set of values of α has been calculated (given in parentheses in Table 3) on the assumption that our value of α for pyridine is exact and by taking the differences between the pK values of pyridine and the picolines from earlier work.[5]

DISCUSSION

The results now reported indicate (i) that the pyridine-catalysed contribution to the rate of hydrolysis of acetic anhydride is proportional to the concentration of free pyridine in solution (Fig. 1) and inversely proportional to the concentration of acetate ion (Fig. 2), (ii) that the rate of the pyridine-catalysed reaction is depressed on going from ordinary water to deuterium oxide as solvent, and (iii) that the conclusions drawn previously [1] from experiments on unbuffered solutions concerning the relative efficiency of pyridine, 2- and

3-picoline, and 2,6-lutidine as catalysts are at least qualitatively correct. The inverse dependence of the catalysed rate on acetate concentration is not evident on casual examination of our data or from experiments in unbuffered media, since the addition of acetate ions also causes an increase in α (the portion of the pyridine base which remains unprotonated in a given solution) as well as exerting a small catalytic effect of its own.

All three results are consistent with the mechanism described by equations (1) and (2), with the specific condition that the second step is the rate-controlling destruction of an unstable intermediate. The inhibiting effect of acetate represents a common-ion effect on the rapidly established equilibrium (1). This mechanism requires the rate law

$$v = \frac{k_1 k_2}{k_{-1}} \cdot \frac{[\mathrm{Py}][\mathrm{Ac_2O}]}{[\mathrm{OAc^-}]},$$

where [Py] represents the spectrophotometrically determined concentration of unprotonated pyridine in solution, and k_1, k_{-1}, and k_2 are the rate coefficients of the respective steps, the concentration of solvent being taken as unity. The final values of $[\mathrm{OAc}](k - k_{\mathrm{Buffer}})/[\mathrm{Py}]_{\mathrm{free}}$ evaluated in Tables 2(b and c) for water and deuterium oxide as solvent therefore represent the ratio k_1k_2/k_{-1}. The solvent isotope-effect on this ratio [*i.e.*, $(k_1k_2/k_{-1})_{\mathrm{H_2O}}/(k_1k_2/k_{-1})_{\mathrm{D_2O}}$] is found to have a value of 5 ± 1, where the indicated limits of uncertainty express an estimate of the accumulated errors in the final result. The equilibrium constant of reaction (1), *i.e.*, k_1/k_{-1}, is expected to be only slightly affected by the isotopic solvent change, so that the large isotope effect reflects in the main a large value of $(k_2)_{\mathrm{H_2O}}/(k_2)_{\mathrm{D_2O}}$. This isotope effect may arise from causes similar to those suggested as explanation of the solvent isotope-effect in the spontaneous hydrolysis of acetic anhydride,[4] but it is as yet not possible to give an exact interpretation of the value found. A large isotope effect in the hydrolysis of the acetylpyridinium ion is reasonable on the ground that the spontaneous hydrolyses of two similar molecules, 1-acetylimidazole and 1-acetylpyrazole, show similar effects, $k_{\mathrm{H}}/k_{\mathrm{D}}$ being 2·5 in the former case[10] and 3·4 in the latter.[11]

The catalytic effect exerted by the four pyridine bases studied clearly separates them into the two categories previously suggested. According to our earlier work, high catalytic activity is associated with absence of α-substituent groups. The more precise conditions of the present experiments allow more definite conclusions. It now appears that 2-picoline and 2,6-lutidine do not produce any significant catalytic effect. This conclusion is less certain in the second case, owing to the extensive—though by no means complete—protonation of lutidine in the solutions employed. It is more certain and more remarkable that even the blocking of a single α-position in pyridine by a methyl group suffices to inhibit the catalytic power, although, towards protons, 2-picoline is a stronger base than pyridine, the ratio of dissociation constants[5] being 5·5. A very small catalytic effect would escape detection, but our measurements indicate that the catalytic coefficient of 2-picoline must be smaller than that of pyridine by a factor exceeding *ca.* 100, *i.e.*, the standard free energies of activation must differ by at least *ca.* 2·8 kcal. mole^{-1}. This factor is thought to reflect in the main the steric effect of α-substitution on the equilibrium constant of reaction (1), and a comparison with other addition reactions of pyridine and 2-picoline which are subject to steric effects may be cited. The dissociation constant of the 2-picoline–trimethylboron adduct is so much greater than that of the corresponding pyridine complex that its value could not be obtained by measurement of the dissociation pressure.[12] In nitrobenzene solution the addition reaction of trimethylboron with 2-picoline is less exothermic than that with pyridine by 5·3 kcal. mole^{-1} and, after allowance for an electronic effect, it is estimated that the steric effect of the 2-methyl group is responsible for a change of *ca.* 5·9 kcal. mole^{-1}. A similar, but smaller, steric

[10] Jencks and Carriuolo, *J. Biol. Chem.*, 1959, **234**, 1272.
[11] Hüttel and Kratzer, *Chem. Ber.*, 1959, **92**, 2014.
[12] Brown and Barbaras, *J. Amer. Chem. Soc.*, 1947, **69**, 1137.

effect on the enthalpy change is deduced in the reaction with boron trifluoride (*ca.* 2·2 kcal. mole^{-1}) and diborane (*ca.* 1·3 kcal. mole^{-1}).[13] If these effects on the enthalpy changes on addition are reproduced in the Gibbs free energies, the results may be compared with the difference in catalytic power in our reaction, and with the difference in free-energy changes on addition of an acetyl cation to pyridine and 2-picoline. The minimum figure of 2·8 kcal. mole^{-1} could therefore be interpreted as implying that the steric requirements of the acetyl group in the 1-acetylpyridinium ion exceed those of $-\overline{B}F_3$ and $-\overline{B}H_3$ in the corresponding adducts.

KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, April 4th,* 1961.]

[13] Brown, *J. Chem. Educ.*, 1959, **36**, 424; Gold, in "Progress in Stereochemistry," Vol. III, ed. Klyne and de la Mare, Butterworths, London, in the press.

---

860. *Thermodynamics of Ion Association. Part VIII.*[1] *Some Transition-metal Malonates.*

By V. S. K. NAIR and G. H. NANCOLLAS.

Thermodynamic equilibrium constants for the association in aqueous solution of nickel, cobalt, and manganese ions with the malonate ion have been determined at various temperatures between 0° and 45° from the e.m.f.s of cells H_2,Pt|H_2Mal,NaOH,MCl_2|AgCl/Ag (Mal = malonate). ΔG, ΔH, ΔS, and ΔC_p are evaluated for the reaction $M^{2+} + Mal^{2-} \rightleftharpoons MMal$, and these are discussed.

PART VII of this series [1] was concerned with the study of the stable five-membered ring chelate compounds formed between nickel, cobalt, and manganese ions and oxalate ion. The investigation has now been extended to the malonate complexes which contain less stable six-membered rings. The malonates do not suffer from the disadvantage of very low solubilities, and it has been possible to make measurements over a wider concentration range than with the oxalates, by using the cell:

(1) $$H_2Pt|H_2Mal(m_1),NaOH(m_2),MCl_2(m_3)|AgCl/Ag$$

EXPERIMENTAL

"AnalaR" salts were used where available and solutions were made up by weight with conductivity water. Malonic acid was recrystallised from 1 : 1 ether–benzene containing 5% of light petroleum (b. p. 60—80°) and was dried *in vacuo* at 40—50° (Found: H, 4·0; C, 34·8. Calc. for $C_3H_4O_4$: H, 3·9; C, 34·6%). The e.m.f. apparatus and experimental procedure have been described previously.[1,2]

RESULTS AND DISCUSSION

It was necessary to determine the primary dissociation constant of malonic acid at the temperatures to be used. Measurements were made with the cell

$$H_2Pt|H_2Mal(m_1),KCl(m_4)|AgCl/Ag$$

for which

$$-\log [H^+] = (E - E^\circ)/k + \log m_4 + \log \gamma_1^2,$$

where m represents molality, γ activity coefficient, and $k = 2{\cdot}3026\,RT/F$. The concentrations of ionic species were obtained from equations for total malonate $m_1 = [H_2Mal] + [HMal^-] + [Mal^{2-}]$, electroneutrality $[H^+] = [HMal^-] + 2[Mal^{2-}]$, the second dissociation

[1] Part VII, McAuley and Nancollas, *J.*, 1961, 2215.
[2] Nair and Nancollas, *J.*, 1958, 4144.

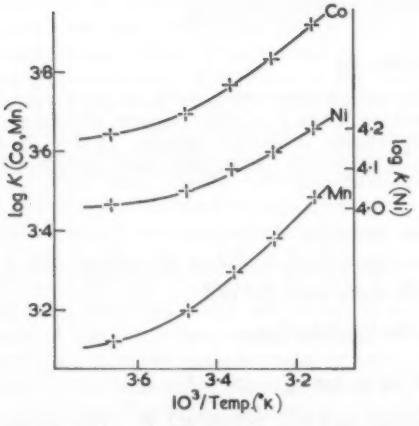
constant [3] $k_2 = [H^+][Mal^{2-}]\gamma_2/[HMal^-]$, and ionic strength $I = [H^+] + [Mal^{2-}] + m_4$. k_1 ($=[H^+][HMal^-]\gamma_1^2/[H_2Mal]$) was calculated by successive approximation of I with use of the activity coefficient expression [4] $-\log \gamma_z = Az^2[I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) - 0{\cdot}2I]$, and the results are given in Table 1. k_1 at 25° agrees well with $1{\cdot}4 \times 10^{-3}$ obtained by Jeffrey and Vogel from conductivity measurements.[5]

TABLE 1.

Primary dissociation constant of malonic acid.

Experiment		1	2	3	4
$10^3 m_1$		2·6185	5·1880	7·3493	10·5587
$10^3 m_4$		7·8490	9·5991	8·9302	9·0812

Temp.	Expt.	$(E - E^\circ)/k$	$10^3[H^+]$	$10^3 I$	$10^3[HMal^-]$	$10^3 k_1$
0°	1	5·0460	1·390	9·242	1·384	1·29
	2	4·7709	2·189	11·79	2·183	1·28
	3	4·7061	2·743	11·68	2·736	1·31
	4	4·6069	3·394	12·48	3·388	1·29
					Mean	1·29
15	1	5·0377	1·424	9·276	1·418	1·38
	2	4·7608	2·253	11·86	2·247	1·38
	3	4·6952	2·814	11·75	2·808	1·40
	4	4·5964	3·499	12·58	3·492	1·38
					Mean	1·38
25	1	5·0345	1·440	9·292	1·434	1·43
	2	4·7571	2·282	11·88	2·276	1·43
	3	4·6913	2·853	11·786	2·846	1·44
	4	4·5921	3·548	12·63	3·542	1·42
					Mean	1·43
35	1	5·0356	1·442	9·294	1·436	1·43
	2	4·7578	2·288	11·89	2·283	1·43
	3	4·6921	2·859	11·79	2·853	1·44
	4	4·5925	3·562	12·64	3·556	1·43
					Mean	1·43
45	1	5·0402	1·433	9·285	1·428	1·40
	2	4·7621	2·277	11·88	2·271	1·40
	3	4·6960	2·847	11·78	2·842	1·42
	4	4·5957	3·552	12·63	3·546	1·41
					Mean	1·41



Plots of K against T^{-1}. (Right-hand ordinates refer to Ni.)

E.m.f.s of cell (I) were measured over a range of concentration, and the thermodynamic association constants $K = \{MMal\}/\{M^{2+}\}\{Mal^{2-}\}$ were calculated as described in Part VII.

[3] Hamer, Burton, and Acree, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 292.
[4] Davies, *J.*, 1938, 2093.
[5] Jeffrey and Vogel, *J.*, 1935, 21.

TABLE 2.

E.M.F. measurements.

Ni malonate

Experiment	1	2	3	4	5	6
10^3m_1	6·9953	8·8309	8·6658	9·3783	9·3888	7·3344
10^3m_2	7·0910	8·9586	8·9599	9·4576	12·279	10·138
10^3m_3	6·7447	8·9607	8·3882	10·1045	7·7463	9·0442

Expt.	$(E - E^\circ)$	10^3I	10^4[H$^+$]	10^3[HMal$^-$]	10^5[Mal^{2-}]	10^3[MMal]	$10^{-4}K$
			At 0°				
1	0·29919	24·15	2·994	4·901	6·277	1·182	1·09
2	0·28985	31·54	3·465	6·020	7·120	1·571	1·09
3	0·29961	29·85	3·056	5·998	7·930	1·654	1·02
4	0·28623	35·23	3·666	6·359	7·320	1·660	1·04
5	0·32227	26·58	0·9893	5·749	22·80	3·086	0·98
6	0·31968	28·72	0·9554	4·023	16·86$_5$	2·925	0·99
						Mean	1·03 ± 0·04
			At 15°				
1	0·31503	24·21	3·088	4·953	6·193$_5$	1·161$_5$	1·11
2	0·30447	31·54	3·678	6·037	6·781	1·577	1·19
3	0·30904	29·87	3·220	6·026	7·620	1·552	1·09
4	0·30067	35·27	3·860	6·396	7·057	1·653	1·11
5	0·33876	26·55	1·046	5·756$_5$	21·75	3·096	1·06
6	0·33612	28·66	1·006	4·008	16·05	2·955	1·09
						Mean	1·11 ± 0·02
			At 25°				
1	0·32539	24·20	3·176	4·958	5·779	1·168	1·22
2	0·31444	31·53	3·790	6·042	6·325	1·584	1·32
3	0·31917	29·83	3·342	6·018	7·035	1·577	1·24
4	0·31052	35·28	3·975	6·419	6·606	1·641	1·21
5	0·34994	26·50	1·075	5·760	20·27	3·395	1·35
6	0·34714	28·62	1·037	4·007	14·91	2·978	1·21
						Mean	1·26 ± 0·04
			At 35°				
1	0·33604	24·16	3·220	4·945$_5$	5·306	1·180	1·37
2	0·32474	31·48	3·843	6·027	5·814	1·599$_5$	(1·48)
3	0·32960	29·78	3·392	6·003	6·459	1·584	1·38
4	0·32065	35·20	4·040	6·384	6·047	1·678$_5$	1·39
5	0·36137	26·41	1·093$_5$	5·753	18·61$_5$	3·128	1·31
6	0·35842	28·56	1·057	4·001	13·67	2·984	1·36
						Mean	1·36 ± 0·03
			At 45°				
1	0·34702	24·11	3·231	4·928	4·776	1·195	1·59
2	0·33533	31·42	3·861	6·002	5·230	1·619	(1·71)
3	0·34032	29·71	3·411	5·978	5·806	1·603	1·60
4	0·33112	35·13	4·055	6·357	5·443	1·698	1·60
5	0·37295	26·32	1·105	5·739	16·64	3·159	1·52
6	0·36982	28·48	1·072	3·990$_5$	12·18	3·005	1·57
						Mean	1·58 ± 0·02

Co malonate

Expt.	1	2	3	4	5	6	7
10^3m_1	7·4816	4·1495	6·9985	8·5901	13·088	8·7848	12·934
10^3m_2	13·055	7·3552	10·211	12·738	18·767	12·977	18·574
10^3m_3	5·8042	2·0758	5·8160	7·2657	9·7605	7·0612	9·2960

Expt.	8	9	10	11	12	13	14
10^3m_1	7·0661	16·427	6·7301	8·7975	8·0952	8·8666	13·016
10^3m_2	10·385	27·950	9·6357	11·997	9·7797	12·257	18·856
10^3m_3	5·5537	11·472	4·8647	6·8558	5·4218	7·0831	9·3630

Expt.	$(E - E^\circ)$	10^3I	10^6[H$^+$]	10^3[HMal$^-$]	10^3[Mal^{2-}]	10^3[MMal]	$10^{-3}K$
			At 0°				
1	0·40023	19·69	4·640	1·893	1·491	4·092	4·68
2	0·44449	10·47	1·860	0·9397	1·628	1·581	4·43
3	0·36281	20·19	22·78	3·664	0·5914$_5$	2·694	4·31
5	0·34301	34·09	33·58	7·111	0·8856	4·959	4·45
7	0·34637	32·99	3·015	7·028	0·9666	4·822	4·19
8	0·36734	19·63	1·962	3·643	0·6785	2·702	4·07
						Mean	4·36 ± 0·15

TABLE 2. (*Continued.*)

Expt.	$(E - E^\circ)$	10^3I	10^6[H$^+$]	10^3[HMal$^-$]	10^3[Mal^{2-}]	10^3[MMal]	$10^{-3}K$
			At 15°				
1	0·42118	19·40	4·862	1·893	1·426	4·157	5·26
2	0·46867	10·40	1·883	0·9398	1·608	1·601	4·82
4	0·37518	24·48	25·46	4·300	0·6539	3·578	4·93
5	0·36025	33·87	36·07	7·110	0·8302	5·016	5·01
6	0·37773	24·28	2·362	4·456	0·7292	3·543	4·57
7	0·36404	32·75	3·236	7·027	0·9064	4·883	4·71
8	0·38599	19·47	2·097	3·642	0·6368	2·745	4·57
9	0·39489	38·70	7·744	4·860	2·742	8·807	5·10
						Mean	4·87 ± 0·20
			At 25°				
2	0·48566	10·24	1·836	9·400	1·572	1·636	5·50
4	0·38726	24·26	26·53	4·298	0·5996	3·634	5·63
5	0·37190	33·60	37·47	7·109	0·7648	5·083	5·69
9	0·40875	38·24	7·733	4·861	2·628	8·921	5·73
10	0·39819	17·35	24·88	3·702	$0{\cdot}5086_5$	2·470	5·84
11	0·37511	24·25	45·10	5·306	0·4353	2·933	5·80
12	0·36553	21·12	81·06	5·833	0·2574	1·756	5·87
13	0·37609	24·75	42·13	5·208	0·4597	3·086	5·72
14	0·37584	32·18	33·31	6·913	0·8267	5·162	5·81
						Mean	5·73 ± 0·10
			At 35°				
1	$0{\cdot}45067_5$	18·81	4·843	1·894	1·272	4·312	6·92
2	$0{\cdot}50330_5$	10·09	1·747	0·9404	1·534	1·674	6·36
4	0·39868	23·95	28·23	4·290	0·5243	3·714	6·84
5	0·38268	33·20	39·83	7·092	0·6700	5·187	6·91
10	0·41105	17·16	25·42	3·699	0·4631	2·518	6·76
11	0·38720	24·08	46·14	5·301	0·3968	2·974	6·64
12	0·37728	21·00	83·33	5·822	0·2332	1·788	6·77
13	0·38861	24·62	42·46	5·208	0·4260	3·120	6·42
14	0·38799	31·90	34·18	6·909	0·7585	5·232	6·77
						Mean	6·71 ± 0·16
			At 45°				
1	0·46590	18·39	4·750	1·894	1·167	4·416	8·37
2	0·52145	9·84	1·638	0·9404	1·472	1·737	8·20
4	0·41052	23·65	29·51	4·282	0·4522	3·791	8·40
5	0·39435	32·82	41·42	7·077	0·5818	5·284	8·44
9	0·43752	36·97	7·422	4·863	2·234	9·238	7·98
10	0·42410	16·95	25·79	3·696	$0{\cdot}4117_5$	2·571	8·06
11	0·39919	23·88	47·34	5·291	$0{\cdot}3492_5$	3·028	7·93
12	0·38908	20·86	85·09	5·805	0·2060	1·788	7·81
14	0·40034	31·55	34·51	6·903	0·6735	5·321	7·94
						Mean	8·12 ± 0·20

Mn malonate

Expt.	1	2	3	4	5	6
10^3m_1	9·7405	4·9059	13·203	17·155	5·4812	12·251
10^3m_2	14·747	9·1704	21·641	32·661	8·3848	17·950
10^3m_3	8·0559	6·0045	10·124	13·708	5·0717	8·4660

Expt.	7	8	9	10	11
10^3m_1	8·8670	$16{\cdot}797_5$	7·7085	8·0905	13·903
10^3m_2	$13{\cdot}092_5$	28·171	9·4930	10·452	14·701
10^3m_3	7·1210	11·220	9·1815	10·215	$14{\cdot}018_5$

Expt.	$(E - E^\circ)$	10^3I	10^5[H$^+$]	10^3[HMal$^-$]	10^4[Mal^{2-}]	10^3[MMal]	$10^{-3}K$
			At 0°				
1	0·37534	31·30	1·019	4·671	1·876	3·167	1·26
2	0·42751	21·06	0·1419	0·6375	1·668	2·600	1·38
3	0·38229	39·90	0·6233	4·733	3·313	5·144	1·30
4	0·41632	55·03	0·1135	1·647	6·943	8·565	1·20
9	0·33713	33·20	4·567	5·594	0·5088	1·464	1·40
						Mean	1·31 ± 0·06
			At 15°				
1	0·39353	30·57	1·128	4·668	1·695	3·350	1·56
2	0·45045	20·92	0·1459	0·6388	1·633	2·634	1·47
3	0·40114	38·77	0·6825	4·731	3·030	5·428	1·62
4	0·43783	53·51	0·1206	1·647	6·562	8·945	1·46

TABLE 2. (*Continued.*)

Expt.	$(E - E^\circ)$	10^3I	$10^5[H^+]$	$10^5[HMal^-]$	$10^4[Mal^{2-}]$	$10^3[MMal]$	$10^{-3}K$
			At 15°				
5	0·41062	19·21	0·8506	2·545	1·094	$1·830_5$	1·53
6	0·38794	34·07	1·365	6·449	1·994	3·763	1·58
7	0·39373	27·50	1·248	4·569	1·459	2·809	1·57
8	0·40447	45·58	0·5509	$5·389_5$	4·480	6·913	1·66
						Mean	1·56 ± 0·05
			At 25°				
5	0·42385	18·83	0·8872	2·545	0·9987	1·926	1·83
6	0·40051	33·41	1·417	6·448	1·831	3·927	1·89
7	0·40643	27·01	1·299	4·568	1·337	2·931	1·87
8	0·41841	44·64	0·5551	5·390	4·247	$7·146_5$	1·95
9	0·36378	32·76	5·444	5·569	$4·095_5$	1·580	2·01
10	0·36661	35·58	$4·433_5$	5·448	5·033	2·021	2·03
						Mean	1·93 ± 0·07
			At 35°				
5	0·43672	18·35	0·9347	2·543	0·8795	2·046	2·32
6	0·41321	36·70	1·461	6·445	1·653	4·107	2·31
7	0·41871	26·37	1·370	4·564	1·178	3·093	2·35
8	0·43236	43·36	0·5581	5·390	3·926	7·467	2·41
9	0·37491	32·56	5·697	5·555	3·650	1·632	2·39
10	0·37779	35·34	4·646	5·437	4·480	2·083	2·41
						Mean	2·37 ± 0·04
			At 45°				
5	0·45009	17·90	0·9647	$2·541_5$	0·7666	2·160	2·94
6	0·42573	31·82	1·514	6·440	1·437	4·326	2·97
7	0·43140	25·75	1·420	4·561	1·024	3·249	2·98
9	0·38634	32·36	5·886	$5·540_5$	3·194	1·686	2·91
10	0·38922	35·09	4·816	5·424	3·906	2·148	2·94
11	0·34622	52·21	17·90	11·09	2·426	1·653	3·03
						Mean	2·96 ± 0·03

Concentrations were chosen so as to exclude complex species of the type $MHMal^+$ which have very much smaller association constants.[6] The results are given in Table 2 which shows the good constancy of K. At 25°, the values are in excellent agreement with $K(NiMal) = 1·3 \times 10^4$, $K(CoMal) = 5·3 \times 10^3$, and $K(MnMal) = 1·95 \times 10^3$ obtained from colorimetric pH measurements.[7] Plots of log K against T^{-1} in Fig. 1 show marked curvatures and, as was found with the oxalates, ΔC_p values are considerable. The equation $\log K = a + bT + cT^2$ fits the results with a maximum difference between calculated and experimental K values of 3%. The values of the parameters calculated from results at 0°, 15°, and 45° are:

	a	-10^2b	10^5c
NiMal	8·821	3·549	6·548
CoMal	10·117	4·923	9·341
MnMal	9·119	4·759	9·378

The thermodynamic properties, ΔG $(= -\boldsymbol{R}T \ln K)$, ΔH $(=2·303\boldsymbol{R}T^2[b + 2cT])$, ΔC_p $(=4·606\boldsymbol{R}T[b + 3CT])$, and ΔS $(=[\Delta H - \Delta G]/T)$ are given in Table 3. Uncertainties were estimated by using different combinations of experimental results at three temperatures for the calculation of a, b, and c. $-\Delta G$ is consistently lower than the

TABLE 3.

Thermodynamic properties.

Reaction	ΔH (kcal. mole^{-1})	ΔG_{298} (kcal. mole^{-1})	ΔS (cal. deg.$^{-1}$ mole^{-1})	ΔC_p (cal. deg.$^{-1}$)
$Ni^{2+} + Mal^{2-}$	1·77 ± 0·1	−5·60 ± 0·02	24·8 ± 0·3	46 ± 20
$Co^{2+} + Mal^{2-}$	2·57 ± 0·1	−5·13 ± 0·02	25·8 ± 0·3	68 ± 25
$Mn^{2+} + Mal^{2-}$	3·53 ± 0·2	−4·48 ± 0·02	26·8 ± 0·7	92 ± 30

corresponding oxalate values and reflects the lower stability of the six-membered ring. A larger ΔH for the malonates, however, makes ΔS almost the same as that for the oxalates.

[6] Cannan and Kibrick, *J. Amer. Chem. Soc.*, 1938, **60**, 2314.
[7] Stock and Davies, *J.*, 1949, 1371.

XUM

The calculation of the entropy of hydration of the complexes from

$$\Delta S_{hyd}(MMal) = \Delta S - \Delta S_g + \Delta S_{hyd}(M^{2+}) + \Delta S_{hyd}(Mal^{2-}),$$

where ΔS_g and ΔS_{hyd} are gaseous and hydration entropies, respectively, was made as described in Part VII; the values are given in Table 4. ΔS_{hyd}(MMal) is lower than the

TABLE 4.

Entropies (in cal. deg.$^{-1}$ mole^{-1}).

Ion pair	S_g (MMal)	ΔS	$S°$ (MMal)	$-\Delta S_{hyd}$ (MMal)	r_+^{-1} (Å^{-1})
NiMal	70·3	24·8	7·3	63·0	1·37
CoMal	70·3	25·8	9·3	61·0	1·35
MnMal	70·2	26·8	12·3	57·9	1·28

corresponding oxalate values (−54·8 to −56·1 cal. deg.$^{-1}$ mole^{-1}) and this may be due to a greater neutralisation of charge accompanying the formation of the oxalate complexes. Frequently association entropies are correlated with properties of the ions taking part in the reactions, no corrections being made for the different translation and rotational entropy contributions. The importance of using only the hydration entropies of the ion-pairs in such comparisons [8] is seen in Table 4. The small changes in ΔS_{hyd}(MMal) are in the expected direction with r_+^{-1} even though ΔS varies in the opposite sense.

Changes in ΔH account for the differences of stability over the series of cations and, as with the oxalates, there is a regular change in ΔH in reverse order to changes in ionisation potential I_{02}, r_+^{-1}, and $-\Delta H_{hyd}(M^{2+})$.

We thank Wilmot Breedon for the award of a fellowship to V. S. K. N., and Mr. I. R. Desai for assistance with some of the experimental work.

COLLEGE OF ADVANCED TECHNOLOGY, GOSTA GREEN, BIRMINGHAM, 4.
CHEMISTRY DEPARTMENT, THE UNIVERSITY, GLASGOW, W.2. [*Received, April 13th*, 1961.]

[8] Nancollas, *Quart. Rev.*, 1960, **14**, 402.

---

861. *Amino-acids of the Cyclohexane Series. Part I.*

By L. MUNDAY.

Several alkyl-1-aminocyclohexanecarboxylic acids have been synthesised by the Bucherer hydantoin and the Strecker synthesis. While the latter synthesis leads to one geometrical isomer in each case, the former gives both possible isomers, the opposite geometric isomer greatly preponderating.[1] Evidence is presented for the configurations assigned, which are based on the resistance to hydrolysis of the 1-amino-4-t-butyl- and -4-isopropyl-cyclohexanenitrile hydrochlorides, on infrared spectra, and on the dissociation constants of the amino-acids.

STERIC hindrance to the hydration of cupric chelate derivatives of α-amino-acids has a marked effect on their solubilities in water.[2] Further illustration of this effect required the synthesis of 2-, 3-, and 4-alkyl-1-aminocyclohexanecarboxylic acids; these were prepared from the corresponding ketones by the Strecker and the Bucherer synthesis. 1-Aminocyclohexanecarboxylic acid has been prepared by the Strecker route by numerous workers, the yields (where quoted) being poor (~10%).[3] In the present work, the yields varied from 15% to 20%.

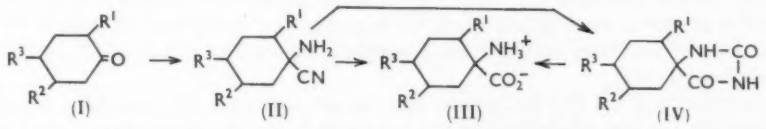
The 2-, 3-, and 4-methyl derivatives were also prepared by both methods, the yields

[1] Preliminary note, Munday, *Nature*, 1961, **190**, 1103.
[2] Graddon and Munday, *Chem. and Ind.*, 1959, 122.
[3] Baddar and Iskander, *J.*, 1954, 203.

being much better by the hydantoin route. In the Strecker synthesis the intermediate 1-amino-3- and -4-methylcyclohexanenitrile hydrochlorides were readily hydrolysed to the corresponding amino-acids by 20% hydrochloric acid at 100° in 10 hours; 1-amino-2-methylcyclohexanenitrile required heating with concentrated hydrochloric acid in a sealed tube at 140° for 10 hours, as Skita and Levi reported;[4] this resistance to hydrolysis seems to be an obvious result of the direct spatial effect of the adjacent 2-methyl group.

But resistance to hydrolysis of the amino-nitrile hydrochlorides was also encountered with higher homologues such as the 4-isopropyl and the 4-t-butyl derivatives where the direct spatial effect is not possible. The explanation of this unexpected effect[5] provided a clue to the configuration of the Strecker products. Hydrolysis of these compounds was achieved by 60% sulphuric acid at 140° in 12 hours.

The Bucherer hydantoin synthesis was applied in the synthesis of higher homologous cyclohexane amino-acids substituted in the 2- or the 4-position.



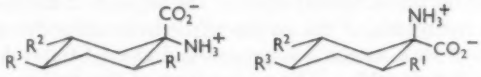
Several workers have made the 2-, 3-, and 4-methyl derivatives by the hydantoin route, and have assumed the identity of these products with those of the Strecker synthesis, presumably on the basis that the hydantoins (IV) are synthesised from the same amino-nitriles (II) involved in the Strecker synthesis, as suggested by Bucherer and Steiner.[6]

No work has been published on the stereochemistry of the substituted 1-aminocyclohexanecarboxylic acids produced by the two methods. We found the Strecker synthesis to produce only one geometrical isomer, since the crude product yielded only one spot on a paper chromatogram. The crude Bucherer product yielded two spots, one at a different and a much weaker one at the same R_F value as that of the Strecker product. Further differences in properties which show the non-identity of the two products are as follows: (1) The 1-amino-4-methyl-, 4-ethyl-, -4-isopropyl-, and -4-t-butyl-cyclohexanecarboxylic acids produced by the Strecker route are anhydrous when crystallised from 50% acetic acid and dried at 120°/25 mm. The corresponding acids made by the Bucherer route are hemi-hydrated on similar treatment, and the water of crystallisation is removed only with difficulty. (2) The melting points of the isomeric amino-acids are different, as are those of the acetyl and benzoyl derivatives of the 2- and 4-methyl compounds. The 3- and 4-methyl compounds made by the Strecker synthesis are converted by heating them with potassium cyanate solution into the ureido-acids and these in refluxing 10% hydrochloric acid yield hydantoins. The melting points of these hydantoins are different from those of the hydantoins produced directly from 3- and 4-methylcyclohexanone by Bucherer's synthesis. The 1-amino-2-methylcyclohexanecarboxylic acid produced by the Strecker synthesis could not be converted into a hydantoin by this method. (3) The infrared spectra of the corresponding amino-acids of the two series, determined for potassium chloride discs, are different, especially in the region 6—8 μ. Thus, in the case of the 2-methyl derivatives, the Strecker products alone give well-defined amino-acid bands. To ensure that the differences in the 4-alkyl compounds are not due to the presence of the half-molecule of water the 4-methyl compound was dehydrated. This necessitated heating the hemi-hydrate at 190°/0·01 mm. for 12 hours. Differences in the spectra still existed. (4) The R_F values on Whatman 3 MM. paper with butan-1-ol–acetic acid–water as eluant are different.

Evidence for the geometrical configuration of the 4-alkyl derivatives was first indicated

[4] Skita and Levi, *Ber.*, 1908, **41**, 2925.
[5] Munday, *Chem. and Ind.*, 1960, 1057.
[6] Bucherer and Steiner, *J. prakt. Chem.*, 1934, **140**, 291.

by the resistance to hydrolysis of the intermediate 1-amino-4-t-butyl- and -4-isopropyl-cyclohexanenitrile hydrochlorides obtained in the Strecker synthesis.[5] This suggested that the nitrile group is in the axial position (cf. V), the normal flexibility of the cyclohexane ring being restricted by the large alkyl groups so that transformation into the alternative chair form is energetically unfavourable. These assignments are supported by the



(V) Strecker product (VI) Hydantoin product

infrared spectra. The 2- and 4-alkyl-acids made by the Strecker reaction give strong and well-resolved bands at 6·2 and 6·5 μ which have been ascribed to N–H deformational modes.[7] These bands are weak and not well resolved in the spectra of the hydantoin products, especially for the 2-methyl (II; $R^2 = R^3 = H$, $R^1 = Me$) and 4-t-butyl derivative (II; $R^1 = R^2 = H$, $R^3 = Bu^t$), which could be explained by restriction of their N–H bond deformations in the more crowded axial position, especially for 1-amino-2-methylcyclohexanecarboxylic acid.

Measurements of the first and second dissociation constants, pK_1' and pK_2', were made. Unfortunately the low solubilities of the 4-isopropyl- and 4-t-butyl derivatives (even in

TABLE 1.

p*K*'s of 1-aminocyclohexanecarboxylic acids.

Acid	pK_1'	pK_2'	pK_1'	pK_2'	Acid	pK_1'	pK_2'	pK_1'	pK_2'
Unsubst.	2·27	9·85							
	Strecker product		Hydantoin product			Strecker product		Hydantoin product	
4-Me	2·53	9·40	2·25	9·78	2-Pr^n			2·55	10·17
4-Et	3·33	9·585	2·74	9·93	2-Pr^i-5-Me			2·58	10·10
3-Me	2·67	9·59	2·23	10·06	2-Bu^n			2·20	9·92
2-Me	2·25	9·675	2·02	9·795	1-Aminocyclopentane-carboxylic acid	2·54	10·33		
2-Et	2·96	10·30	2·30	10·18	1-Aminocycloheptane-carboxylic acid	2·67	9·78		

acid or alkaline media, and also in dimethylformamide) prevented determination of their acidity constants by this method. The first dissociation constants (which refer to the ionisation of the carboxyl group) for the 2- and 4-alkyl-hydantoin products are greater than for the isomeric Strecker products. This supports the belief that the carboxyl group is preferentially equatorial in the hydantoin product, and axial in the Strecker product. The difference in dissociation constants is usually ascribed to the greater ionic solvation possible in the equatorial position, which stabilises the carboxylate ion.[8] The second dissociation constant, referring to the loss of a proton by the substituted ammonium ion, is weaker for the 2- and 4-alkyl Bucherer products. This is contradictory to available evidence and to accepted principles of conformational analysis. Bird and Cookson [9] have studied the base strengths of epimeric equatorial and axial primary amino- and dimethylamino-groups in various positions of the steroid nucleus and have found that in general axial amino-groups are less basic than their equatorial epimers. The exceptions are readily explicable in terms of intramolecular effects in the steroid molecule. The strength of an axial basic group is considered to be weaker than for the same group in an equatorial position because solvation, which would assist salt formation, is more restricted for the axial group. For the present equilibrium, $^+NH_3{\cdot}R{\cdot}CO_2^- \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} NH_2{\cdot}R{\cdot}CO_2^-$, solvation effect might be less easily interpreted.

[7] Bellamy, "Infra-red Spectra of Complex Molecules," Methuen, London, 1959, p. 238.
[8] Stolow, *J. Amer. Chem. Soc.*, 1959, **81**, 5806.
[9] Bird and Cookson, *J.*, 1960, 2343.

Paper chromatography was used to examine both the pure and the crude amino-acids produced by the two routes. Butan-1-ol–acetic acid (4 : 1) saturated with water was used as ascending eluant. While the crude 3- and 4-methylcyclohexane Strecker products yielded only one spot, the crude hydantoin products gave one strong spot and a much fainter spot at the same R_F value as the isomeric Strecker product. The crude 3- and 4-methylcyclohexane-1-spiro-5′-hydantoins produced by the Bucherer synthesis were analysed by partition chromatography on a cellulose column with butan-1-ol–acetic acid as eluant. About 0·2% of material having the melting point of the opposite isomer was obtained and 99% of the pure main product was recovered. Fractional crystallisation was also applied to determine the proportions of the isomers, and the proportion of the minor constituent found was again about 0·2%.

Experimental

Products were dried at 120°/25 mm. over $CaCl_2$ unless otherwise stated.

1-Aminocyclohexanecarboxylic acid was prepared by a Strecker synthesis from cyclohexanone. Yields averaged 15—20%; the m. p. was 320—325° (decomp.) (Found: C, 58·2; H, 9·0; N, 9·8. Calc. for $C_7H_{13}NO_2$: C, 58·7; H, 9·15; N, 9·8%).

1-*Amino*-cis-4-*methylcyclohexanecarboxylic Acid.*—4-Methylcyclohexanone (45 g., 0·4 mole), potassium cyanide (30 g., 0·4 mole), and ammonium chloride (22·0 g., 0·4 mole) were dissolved in water (300 ml.) and alcohol (250 ml.) and kept at room temperature for 6 days. The dark solution was diluted with water (300 ml.) and saturated with hydrogen chloride. After a further 2 days 1-amino-*cis*-4-methylcyclohexanenitrile hydrochloride (62·2 g., 88%) had crystallised. This hydrochloride (60 g.) was refluxed with 20% hydrochloric acid for 12 hr., the solution evaporated to dryness, and the residue extracted (Soxhlet) with ethanol–ether (9 : 1) for 8 hr. After removal of the solvent, the residue was basified with aqueous ammonia (*d* 0·880), to yield 1-amino-*cis*-4-methylcyclohexanecarboxylic acid (45·5 g.), needles [from acetic acid–water (1 : 1)], m. p. 356—360° (sublimes), R_F 0·69 (Found: C, 61·6; H, 9·7; N, 8·4. Calc. for $C_8H_{15}NO_2$: C, 61·1; H, 9·6; N, 9·0%). The N-*acetyl derivative* crystallised from ethanol–water as needles, m. p. 220—222° (Found: C, 60·1; H, 8·65; N, 6·8. $C_{10}H_{17}NO_3$ requires C, 60·3; H, 8·6; N, 7·0%). The N-*benzoyl derivative*, prepared by heating the amino-acid in pyridine with benzoyl chloride was obtained as needles (from ethanol–water), m. p. 209—210° (Found: C, 68·9; H, 7·6; N, 5·4. $C_{15}H_{19}NO_3$ requires C, 68·9; H, 7·3; N, 5·4%).

cis-4-*Methylcyclohexane*-1-*spiro*-5′-*hydantoin.*—1-Amino-*cis*-4-methylcyclohexanecarboxylic acid (1·0 g.) and potassium cyanate (0·6 g.) in water (10 ml.) were refluxed for 30 min. The cooled solution was acidified with hydrochloric acid, to precipitate the ureido-acid, which was converted without purification by heating it with 20% hydrochloric acid (20 ml.) for 30 min. into cis-4-*methylcyclohexane*-1-*spiro*-5′-*hydantoin*, plates (from ethanol), m. p. 215—216° (Found: C, 58·8; H, 7·4; N, 15·35. $C_9H_{14}N_2O_2$ requires C, 59·3; H, 7·7; N, 15·4%).

1-*Amino*-trans-4-*methylcyclohexanecarboxylic Acid.*—Bucherer's hydantoin synthesis [10] was followed. 4-Methylcyclohexanone (22·4 g., 0·2 mole), potassium cyanide (14·0 g., 0·22 mole), and ammonium carbonate (87 g., 0·9 mole) in water (100 ml.) and ethanol (100 ml.) were heated at 50—55° for 5 hr. and at 90—95° for 1 hr., then kept overnight. *trans*-4-Methylcyclohexane-1-spiro-5′-hydantoin was precipitated (29·8 g., 82%), having m. p. 281—282°. Henze and Speer [11] reported m. p. 279—280°. This hydantoin (10 g.) was heated with 60% sulphuric acid (57 ml.) at 150° for 24 hr. On cooling and dilution with water, a small amount of a pale straw-coloured solid was precipitated. The filtrate was neutralised with barium hydroxide, then made just acid with dilute sulphuric acid, and filtered hot. (If the solution was alkaline much of the amino-acid remained behind, presumably as barium salt.) The filtrate was evaporated to about 20 ml. and neutralised with aqueous ammonia (*d* 0·88), to produce 1-*amino*-trans-4-*methylcyclohexanecarboxylic acid* (8·0 g.). Crystallisation from acetic acid–water (1 : 1) afforded needles, m. p. 305—310° (sublime), R_F 0·57 (Found: C, 57·9; H, 9·8; N, 8·5. $C_8H_{15}NO_2,\frac{1}{2}H_2O$ requires C, 57·8; H, 9·75; N, 8·4%).

In order to remove the water, it was necessary to heat the compound at 190°/0·01 mm. over P_2O_5 for 12 hr. (Found: C, 60·2; H, 9·6. Calc. for $C_8H_{15}NO_2$: C, 61·1; H, 9·6%). The

[10] Bucherer and Lieb, *J. prakt. Chem.*, 1934, **141**, 5.
[11] Henze and Speer, *J. Amer. Chem. Soc.*, 1942, **64**, 522.

XUM

N-*acetyl derivative* crystallised from ethanol water as needles, m. p. 223—224·5° (Found: C, 60·4; H, 8·8; N, 6·8. $C_{10}H_{17}NO_3$ requires C, 60·3; H, 8·6; N, 7·0%). Equal weights of this acetyl derivative and of the acetyl derivative of the *cis*-4-methyl-amino-acid gave, when mixed, m. p. 170—185°. The N-*benzoyl derivative*, prepared as above, formed needles (from ethanol–water), m. p. 234—236° (Found: C, 68·7; H, 7·4; N, 5·2. $C_{15}H_{19}NO_3$ requires C, 68·9; H, 7·3; N, 5·4%).

4-*Ethylcyclohexanone*.—4-Ethylphenol was catalytically hydrogenated to 4-ethylcyclohexanol which was oxidised with potassium dichromate and dilute sulphuric acid to the ketone b. p. 191—194°; von Braun, Mannes, and Reuter [12] record b. p. 192—194°.

1-*Amino*-cis-4-*ethylcyclohexanenitrile Hydrochloride*.—4-Ethylcyclohexanone was converted by the method used for the 4-methyl analogue into the *amino-nitrile hydrochloride*, plates, m. p. 187—190° (decomp.), from ethanol–hydrochloric acid. The crystals were washed with ether, and dried at room temperature *in vacuo* over paraffin wax (Found: C, 56·6; H, 9·2; N, 15·35; Cl, 19·15. $C_9H_{17}N_2Cl$ requires C, 57·3; H, 9·1; N, 14·9; Cl, 18·8%).

1-*Amino*-cis-4-*ethylcyclohexanecarboxylic Acid*.—The amino-nitrile hydrochloride (6·0 g.) was heated with 70% sulphuric acid (16 ml.) at 140° for 18 hr. The dark solution was cooled, poured into water (40 ml.), neutralised with barium hydroxide, made slightly acid with dilute sulphuric acid, and filtered hot. The filtrate was evaporated, then treated with ammonia to precipitate the amino-acid, needles [from acetic acid–water (1 : 1)], m. p. 360—370° (sinter) (Found: C, 63·0; H, 9·3; N, 8·6. $C_9H_{17}NO_2$ requires C, 63·1; H, 10·0; N, 8·2%).

trans-4-*Ethylcyclohexane*-1-*spiro*-5′-*hydantoin*.—4-Ethylcyclohexanone was converted by Bucherer's method [10] in 64% yield into the *hydantoin*, plates (from aqueous ethanol), m. p. 265—266° (Found: C, 61·5; H, 8·0; N, 14·3. $C_{10}H_{16}N_2O_2$ requires C, 61·5; H, 8·2; N, 14·3%).

1-*Amino*-trans-4-*ethylcyclohexanecarboxylic Acid*.—The hydantoin was hydrolysed by 60% sulphuric acid as for the 4-methyl derivative, to the *amino-acid*, needles (from acetic acid–water), m. p. 306—308° (sublime) (Found: C, 60·7; H, 10·45; N, 7·7. $C_9H_{17}NO_2,\frac{1}{2}H_2O$ requires C, 60·0; H, 10·3; N, 7·8%).

4-*Isopropylcyclohexanone, etc.*—This ketone was made from *p*-isopropylphenol *via* the 4-isopropylcyclohexanol as for the 4-ethyl analogue, and had b. p. 125—130°/25 mm. Cahn, Penfold, and Simonsen [13] reported b. p. 139—140°/100 mm. This was converted by the same methods as for the 4-ethylcyclohexanone into 1-*amino*-cis-4-*isopropylcyclohexanenitrile hydrochloride* (92%), plates (from ethanol–hydrochloric acid), m. p. 213—215° (char) (Found: C, 60·0; H, 9·6; N, 13·8; Cl, 17·6. $C_{10}H_{19}N_2Cl$ requires C, 59·2; H, 9·5; N, 13·8; Cl, 17·5%), 1-*amino*-cis-4-*isopropylcyclohexanecarboxylic acid*, plates (from acetic acid–water), m. p. 321—323° (chars) (Found: C, 64·8; H, 10·2; N, 7·4. $C_{10}H_{19}NO_2$ requires C, 64·8; H, 10·4; N, 7·6%), and trans-4-*isopropylcyclohexane*-1-*spiro*-5′-*hydantoin* (78%), plates (from aqueous dioxan), m. p. 300·5—301·5° (Found: C, 62·9; H, 8·6; N, 13·0. $C_{11}H_{18}N_2O_2$ requires C, 62·9; H, 8·6; N, 13·3%).

1-*Amino*-trans-4-*isopropylcyclohexanecarboxylic Acid*.—The hydantoin was hydrolysed with 60% sulphuric acid in a similar manner to the 4-ethyl derivative, but after dilution with water the *amino-acid hydrogen sulphate* was precipitated as a dark grey solid. This, after decolorisation with charcoal in aqueous acetic acid, yielded white plates, m. p. >360° [Found: N, 5·8; SO_4, 20·9. $(C_{10}H_{20}NO_2)_2SO_4$ requires N, 6·0; SO_4, 20·6%]. This on treatment with ammonia yielded the *amino-acid*, plates [from aqueous acetic acid (1 : 1)], m. p. 317—318° (sublime) (Found: C, 62·5; H, 10·6; N, 7·6. $C_{10}H_{19}NO_2,\frac{1}{2}H_2O$ requires C, 61·8; H, 10·4; N, 7·2%).

4-*t*-*Butylcyclohexanone, etc.*—The ketone was obtained by oxidation of commercial 4-t-butylcyclohexanol with potassium dichromate and dilute sulphuric acid, and had b. p. 176—182°/140 mm., m. p. 48—50°. It was converted by the above methods into 1-*amino*-cis-4-*t*-*butylcyclohexanenitrile hydrochloride* (90%), plates (from ethanolic hydrochloric acid), m. p. 320—325° (decomp.) (Found: C, 61·0; H, 9·8; N, 12·8; Cl, 16·5. $C_{11}H_{21}ClN_2$ requires C, 60·95; H, 9·8; N, 13·0; Cl, 16·4%) (recovered unchanged after 20 hours' heating with 20% hydrochloric acid at 100°), 1-*amino*-cis-4-*t*-*butylcyclohexanecarboxylic acid* (by hydrolysis with 65% sulphuric acid at 140° for 40 hr.), plates [from acetic acid–water (1 : 1)], m. p. 345—350° (Found: C, 66·1; H, 10·8; N, 6·9. $C_{11}H_{21}NO_2$ requires C, 66·3; H, 10·6; N, 7·0%), *trans*-4-*t*-*butylcyclohexane*-1-*spiro*-5′-*hydantoin* (~100%), plates (from aqueous ethanol), m. p. 322° (Found: C, 64·7; H, 9·2; N, 12·3. $C_{12}H_{20}N_2O_2$ requires C, 64·3; H, 9·0; N, 12·5%), and 1-*amino*-trans-4-*t*-*butylcyclohexanecarboxylic acid* (by hydrolysis with 70% sulphuric acid to the amino-acid sulphate

[12] von Braun, Mannes, and Reuter, *Ber.*, 1933, **66**, 1499.
[13] Cahn, Penfold, and Simonsen, *J.*, 1931, 1369.

XUM

and treatment with ammonia), plates [from aqueous acetic acid (1 : 1)], m. p. 300—304° (sublime) (Found: C, 63·1; H, 10·2; N, 7·1. $C_{11}H_{21}NO_2,\frac{1}{2}H_2O$ requires C, 63·4; H, 10·6; N, 6·7%).

1-*Amino*-trans-3-*methylcyclohexanecarboxylic Acid*.—3-Methylcyclohexanone (22·5 g., 0·2 mole), potassium cyanide (15·6 g., 0·24 mole), and ammonium chloride (12·7 g., 0·24 mole) in 1 : 1 water–ethanol (200 ml.) were kept for 60 hr. The dark solution was diluted with water (100 ml.), saturated with hydrogen chloride, and refluxed for 16 hr. The solution was evaporated and the residue extracted (Soxhlet) with ethanol–ether (400 ml.; 9 : 1). Removal of the solvent afforded the crude hydrochloride, which on treatment with ammonia yielded the *amino-acid* (5·3 g., 31%), needles (from water), m. p. 360—365° (sublime) R_F 0·73 (Found: C, 60·95; H, 9·8; N, 8·6. $C_8H_{15}NO_2$ requires C, 61·15; H, 9·6; N, 9·0%).

trans-3-*Methylcyclohexane*-1-*spiro*-5′-*hydantoin* was prepared by the action of potassium cyanate on the Strecker amino-acid as for the 4-methyl compound. It formed needles, m. p. 237—238°, from ethanol (Found: C, 59·5; H, 7·9; N, 15·1. $C_9H_{14}N_2O_2$ requires C, 59·3; H, 7·7; N, 15·4%).

cis-3-*Methylcyclohexane*-1-*spiro*-5′-*hydantoin*.—3-Methylcyclohexanone (22·4 g.), potassium cyanide (26 g.), and ammonium carbonate (90 g.) were heated in 1 : 1 aqueous ethanol (200 c.c.) at 50—55° for 5 hr., then for 1 hr. at 90—95°. Next morning the hydantoin was collected (30·8 g., 84%); it formed needles, m. p. 274°, from ethanol. Henze and Speer [11] reported m. p. 268·5—269°.

1-*Amino*-cis-3-*methylcyclohexanecarboxylic Acid*.—The previous hydantoin (20·0 g.) in 70% sulphuric acid (120 ml.) was heated at 140° for 30 hr. The solution was cooled, diluted with water, and neutralised with barium carbonate. After being heated to the b. p. the solution was made just acid with dilute sulphuric acid and filtered. The filtrate was evaporated to ~40 ml. and neutralised with aqueous ammonia (*d* 0·88), to yield the crude *amino-acid*, needles (from water), m. p. 312—315° (sublime) R_F 0·65 (Found: C, 60·5; H, 9·6; N, 9·0. $C_8H_{15}NO_2$ requires C, 61·15; H, 9·6; N, 9·0%).

1-*Amino*-cis-2-*methylcyclohexanenitrile hydrochloride*, prepared by a Strecker synthesis from 2-methylcyclohexanone in 42% yield, had m. p. 192—195° (Found: C, 54·5; H, 9·0; N, 16·1. Calc. for $C_8H_{15}ClN_2$: C, 55·0; H, 8·6; N, 16·4%). Skita and Levi [3] reported m. p. 182°.

1-Amino-*cis*-2-methylcyclohexanecarboxylic Acid.—The amino-nitrile hydrochloride (3·9 g.) and concentrated hydrochloric acid (30 ml.) were heated in 4 sealed tubes at 140° for 10 hr. The tubes were cooled in acetone–solid carbon dioxide before being opened (high pressure). In some experiments, violent explosions occurred when the tubes were opened. Dilution with water (100 ml.) gave an oil that was identified as 2-methylcyclohexanone by its b. p.; the aqueous layer was evaporated to dryness and treated with ammonia, yielding the *amino-acid*, needles (from water), m. p. 355—360° (Skita and Levi [4] reported m. p. >300°), R_F 0·33 with *s*-collidine (see below) (Found: C, 60·6; H, 10·3; N, 8·7. Calc. for $C_8H_{15}NO_2$: C, 61·15; H, 9·6; N, 9·0%). The N-*acetyl derivative* formed needles, m. p. 220—221°, from aqueous ethanol (Found: C, 60·1; H, 8·7. $C_{10}H_{17}NO_3$ requires C, 60·3; H, 8·6%). The N-*benzoyl derivative* formed needles, m. p. 174—175°, from aqueous ethanol (Found: C, 68·55; H, 7·3. $C_{15}H_{19}NO_3$ requires C, 68·9; H, 7·3%). Refluxing the amino-acid (0·6 g.) and potassium cyanate (0·6 g.) in water (25 ml.) for 40 min., then cooling and acidifying the mixture gave 50 mg. of precipitate; this dissolved completely when boiled with dilute hydrochloric acid.

1-*Amino*-trans-2-*methylcyclohexanecarboxylic Acid*.—This was prepared by the method of Connors and Ross,[14] and had m. p. 300°, R_F 0·27 with *s*-collidine. The N-*acetyl derivative* formed prisms, m. p. 181—181·5°, from aqueous ethanol (Found: C, 60·2; H, 8·5. $C_{10}H_{17}NO_3$ requires C, 60·3; H, 8·6%).

2-*Ethylcyclohexanone, etc.*—The ketone was made by oxidation of commercial 2-ethylcyclohexanol with potassium dichromate and dilute sulphuric acid and had b. p. 184—186°. It was converted by the usual methods into trans-2-*ethylcyclohexane*-1-*spiro*-5′-*hydantoin* (97%), plates (from ethanol), m. p. 237—240° (Found: C, 61·7; H, 8·4; N, 14·0. $C_{10}H_{16}N_2O_2$ requires C, 61·4; H, 8·2; N, 14·0%), and 1-*amino*-trans-2-*ethylcyclohexanecarboxylic acid* (by 60% sulphuric acid), plates (from water), m. p. 320° (sublime) (Found: C, 63·3; H, 10·0; N, 8·2. $C_9H_{17}NO_2$ requires C, 63·1; H, 10·0; N, 8·2%).

1-*Amino*-cis-2-*ethylcyclohexanecarboxylic Acid*.—2-Ethylcyclohexanone (20·0 g.), potassium cyanide (30·0 g.), ammonium chloride (25·0 g.) in water (150 ml.) and ethanol (75 ml.) were set

[14] Connors and Ross, *J.*, 1960, 2130.

XUM

aside for 60 hr. The dark solution was diluted with water (200 ml.) and saturated with hydrogen chloride. The solution was evaporated and the residue extracted with ethanol–ether (400 ml.; 9 : 1). From the extract, the crude amino-nitrile hydrochloride was obtained on removal of the solvent, and was hydrolysed with 70% sulphuric acid in 20 hr. to the *amino-acid*, plates (from 50% aqueous acetic acid), m. p. 340° (sinter) (Found: C, 62·7; H, 9·6; N, 8·5. $C_9H_{17}NO_2$ requires C, 63·1; H, 10·0; N, 8·2%).

trans-2-*Propylcyclohexane*-1-*spiro*-5′-*hydantoin* was prepared from the commercially available ketone in 65% yield; it formed plates (from ethanol), m. p. 200—202° (Found: C, 62·8; H, 8·9; N, 13·5. $C_{11}H_{18}N_2O_2$ requires C, 62·9; H, 8·6; N, 13·3%).

1-*Amino*-trans-2-*propylcyclohexanecarboxylic Acid*.—The previous hydantoin was converted by 60% sulphuric acid into the *amino-acid*, needles (from aqueous ethanol), m. p. 301—303° (Found: C, 60·7; H, 10·4; N, 7·7. $C_{10}H_{19}NO_2,\frac{1}{2}H_2O$ requires C, 61·8; H, 10·4; N, 7·2%). The *hydrochloride* formed needles, m. p. 321—323° (sublime), from hydrochloric acid–ethanol (Found: C, 54·4; H, 9·9; N, 6·4; Cl, 17·1. $C_{10}H_{10}ClNO_2$ requires C, 54·2; H, 9·1; N, 6·3; Cl, 16·1%).

trans-2-*Isopropyl*-5-*methylcyclohexane*-1-*spiro*-5′-*hydantoin*.—Prepared in 37% yield from natural (−)-menthone, this *spiran* formed needles (from ethanol), m. p. 228—231·5° (Found: C, 63·0; H, 8·8; N, 11·6. $C_{12}H_{20}N_2O_2,\frac{1}{2}C_2H_5{\cdot}OH$ requires C, 63·1; H, 9·4; N, 11·3%).

1-*Amino*-trans-2-*isopropyl*-5-*methylcyclohexanecarboxylic Acid*.—The previous hydantoin was hydrolysed by 60% sulphuric acid to the *amino-acid*, needles [from water–acetic acid (1 : 1)], m. p. 330° (Found: C, 62·9; H, 10·0; N, 6·1. $C_{11}H_{21}NO_2,\frac{1}{2}C_2H_4O_2$ requires C, 62·9; H, 10·0; N, 6·1%).

trans-2-*Butylcyclohexane*-1-*spiro*-5′-*hydantoin*.—Commercial 2-butylcyclohexanone was converted in 50% yield into the *hydantoin*, plates (from ethanol), m. p. 182—184·5° (Found: C, 63·5; H, 9·5; N, 11·7. $C_{12}H_{20}N_2O_2,\frac{1}{2}C_2H_5{\cdot}OH$ requires C, 63·1; H, 9·4; N, 11·3%).

1-*Amino*-trans-2-*butylcyclohexanecarboxylic Acid*.—The previous hydantoin was hydrolysed to the *amino-acid*, prisms (from aqueous ethanol), m. p. 295—297° (sublime) (Found: C, 66·1; H, 11·1; N, 6·7. $C_{11}H_{21}NO_2$ requires C, 66·3; H, 10·6; N, 7·0%).

Determinations of pK_1' and pK_2' at 20° were made for aqueous solutions of constant ionic strength 0·1. 50 or 25 ml. of 0·01M-solutions of the amino-acids were half-neutralised with 0·01M-hydrochloric acid or 0·05M-sodium hydroxide, and the calculated quantity of " AnalaR " sodium chloride was added. Pure nitrogen was passed through the solution and the pH determined with glass and a calomel electrode in conjunction with a Cambridge pH meter. The value of the pH for the half-neutralisation by hydrochloric acid was corrected for dilution effects by applying the equation,[15] $pK_1' = pH + \log [(\frac{1}{2}c - H^+)/(\frac{1}{2}c + H^+)]$, where c = initial concentration of the base and the values of pH and H^+ are those at the calculated half-neutralisation point. A similar correction for pK_2' was not applied since it was negligible in all cases.

Solubilities at 25° were measured by dissolving a known weight of the amino-acid in distilled water, adding the equivalent amount of sodium hydroxide or hydrochloric acid where necessary, and leaving the whole in a thermostat-bath for 48 hr. The undissolved material was then filtered off and weighed. The results are in Table 3.

TABLE 3.

Solubilities at 25° (g. per 100 ml.).

1-Amino-carboxylic acid	Strecker product	Bucherer product
Cyclohexane-	6·60	
4-Methylcyclohexane-	0·283	0·173
,, ,, Na salt	9·2	8·1
,, ,, hydrochloride	8·7	9·9
4-t-Butylcyclohexane-	0·0023	0·0047
,, ,, Na salt	0·075	0·057
,, ,, hydrochloride	0·035	0·285
2-Methylcyclohexane-	1·20	1·79

Paper chromatograms of the amino-acids were obtained by ascending elution with butan-1-ol–acetic acid (4 : 1) saturated with water as solvent, and sprays of 0·1% ninhydrin in butan-1-ol. No spots were detected for the 1-amino-2-methylcyclohexanecarboxylic acids except by using *s*-collidine as solvent.

[15] Morley and Simpson, *J.*, 1949, 1014.

In a typical experiment involving partition chromatography of the hydantoins, crude 3-methylcyclohexane-1-spiro-5′-hydantoin (8·27 g.), made by the Bucherer procedure, was passed in hot ethanol (100 ml.) on to a powdered cellulose column (57 cm.) saturated with water. Elution was with butan-1-ol–acetic acid (4 : 1) saturated with water; 480 ml. of the solvent were required to elute the pure main product (8·12 g.; m. p. 270°). Immediately after this, 0·016 g. of a product, m. p. 235—240°, was obtained; this was undepressed in m. p. on admixture with the hydantoin produced from the Strecker amino-acid.

The author is deeply indebted to Drs. H. Heaney and J. Rose for much helpful advice and criticism, and to Shell Research Ltd. (Thornton Research Centre) for the determination of the infrared spectra.

SCIENCE DEPARTMENT, BIRKENHEAD TECHNICAL COLLEGE,
BOROUGH ROAD, BIRKENHEAD, CHESHIRE. [*Received, April 14th*, 1961.]

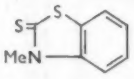
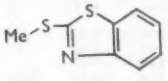
---

862. *The Crystal and Molecular Structure of 3-Methylbenzothiazoline-2-thione.*

By P. J. WHEATLEY.

The crystal and molecular structure of 3-methylbenzothiazoline-2-thione has been determined by two-dimensional *X*-ray diffraction methods. The structure proposed previously on chemical and other physicochemical grounds is confirmed. The dimensions of the molecule have been determined and are compared with those in similar molecules.

THE structure of the 3-methylbenzothiazoline-2-thione molecule (I) was determined chemically by Mills, Clark, and Aeschlimann.[1] Their conclusions were confirmed and extended to the isomeric 2-methylthiobenzothiazole (II) by Morton and Stubbs.[2]

(I)   (II)

Nevertheless recent work on the other physical properties of these and related molecules has led to the belief that the earlier work should be checked. Accordingly a two-dimensional *X*-ray crystallographic study of the higher-melting isomer has been carried out. The earlier work is confirmed in every respect.

TABLE 1.

Fractional atomic co-ordinates.

Atom	*x/a*	*y/b*	*z/c*	Atom	*x/a*	*y/b*	*z/c*	Atom	*x/a*	*y/b*	*z/c*
S_1	0·023	0·404	0·868	C_2	0·175	−0·021	0·569	C_6	0·535	0·522	0·754
S_2	−0·159	0·000	0·708	C_3	0·226	0·490	0·834	C_7	0·481	0·682	0·855
N	0·159	0·150	0·680	C_4	0·280	0·330	0·733	C_8	0·326	0·672	0·896
C_1	0·008	0·165	0·743	C_5	0·435	0·340	0·693				

EXPERIMENTAL

3-Methylbenzothiazoline-2-thione. $C_8H_7NS_2$. M 181·3. Monoclinic. $a = 8·06_8$, $b = 5·67_9$, $c = 9·16_2$ Å, $\beta = 98°\ 36'$. $U = 415$ Å^3. $D_m = 1·44$ (by flotation), $Z = 2$. $D_c = 1·451$, $F(000) = 188$. Space group $P2_1$ (C_2^2, No. 4). Cu-K_α radiation (λ 1·542 Å), single-crystal rotation and Weissenberg photographs.

The lengths of the crystal axes exclude $P2_1/m$ as a possible space group. $P2_1$ was assumed and it is confirmed by the subsequent analysis. Multiple-film Weissenberg photographs were taken round [*b*] and [*a*]. Relative intensities were estimated visually by comparison with

[1] Mills, Clark, and Aeschlimann, *J.*, 1923, 2362.
[2] Morton and Stubbs, *J.*, 1939, 1321.

standard strips prepared from the same crystals. No correction was made for absorption ($\mu = 52{\cdot}1$ cm.$^{-1}$). 135 *h*0*l* and 63 0*kl* reflexions were observed to be non-zero. Each projection was solved from a sharpened Patterson synthesis from which the positions of the two sulphur atoms could readily be located. Successive Fourier syntheses gave the positions of the lighter atoms, and each projection was then refined by difference syntheses. The scattering factors used were those of Berghuis *et al.*[3] for the carbon and nitrogen atoms, and that of Tomiie and Stam [4] for the sulphur atoms. Hydrogen atoms were ignored. An isotropic temperature factor $B = 4{\cdot}66$ Å^2 proved satisfactory for each projection. The final agreement index was $R = 10{\cdot}7\%$ for the *h*0*l* and $R = 10{\cdot}6\%$ for the 0*kl* projection. These agreement indices refer to the observed terms only.

Results

The co-ordinates of the atoms are given in Table 1, and the observed and calculated structure factors in Table 2. Figs. 1(*a* and *b*) show the final Fourier maps of the *h*0*l* and

Table 2.

Observed and calculated structure factors for one asymmetric unit.

hol	F_o	F_c	*hol*	F_o	F_c	*hol*	F_o	F_c	*hol*	F_o	F_c	*hol*	F_o	F_c
0.0.1	4·88	6·39	7	0·85	1·26	6	1·11	−1·56	9	0·85	−0·57	8	2·67	−3·49
2	30·33	−32·93	8	3·12	2·54	7	1·35	1·81	10	2·95	−3·65			
3	0·92	−1·31	9	2·40	2·89				11	0·84	−0·80	$\bar{6}$.0.1	2·64	−2·50
4	3·43	−3·17				7.0.3	6·29	6·09				2	7·27	−6·75
5	14·28	−15·05	3.0.1	10·70	10·92	5	4·11	−4·41	$\bar{5}$.0.1	14·87	14·23	3	0·82	−0·68
7	10·56	11·26	2	8·00	8·51	6	1·10	−1·26	2	7·97	6·97	5	3·11	−3·59
8	2·12	1·42	3	5·28	−5·97				3	15·32	−15·83	6	1·95	0·93
11	1·13	−0·96	4	3·51	−4·59	8.0.1	2·04	1·48	4	8·61	−8·64	7	4·25	4·74
			5	2·69	−2·07				5	5·29	5·40	9	0·96	−0·71
1.0.0	17·66	15·80	6	3·56	−3·17	9.0.1	1·67	1·61	7	2·22	−2·58			
2	6·49	6·83	7	0·87	−1·34	2	1·99	2·46	8	7·27	6·48	$\bar{7}$.0.1	1·50	−2·00
3	8·99	−7·90	8	3·57	4·21				9	1·46	1·51	2	7·52	−7·61
4	7·71	6·82				10.0.1	1·75	1·78	10	2·77	−2·90	3	2·12	−1·89
5	6·63	6·32	4.0.1	13·69	13·65				11	0·79	−0·78	4	2·61	3·08
6	10·29	10·19	2	2·98	2·87	$\bar{1}$.0.1	9·34	−9·72				5	0·86	−1·16
7	6·71	5·66	3	11·54	−11·78	2	9·76	−10·21	$\bar{4}$.0.1	2·67	1·79	6	1·44	1·03
10	0·92	−0·87	5	3·23	2·46	3	12·18	−10·45	2	7·42	−7·39	7	3·31	3·19
			6	3·12	−3·14	4	0·78	0·78	3	8·29	−7·66			
1.0.1	10·78	11·00	7	1·48	−1·52	5	2·64	−2·02	4	8·20	−7·93	$\bar{8}$.0.2	2·24	−1·53
2	2·32	3·00	8	3·49	4·12	6	1·79	1·03	6	3·55	3·94	3	2·79	−2·78
3	7·21	7·07				7	5·39	5·44	7	6·32	5·63	7	2·05	1·48
4	7·24	−8·39	5.0.1	8·60	7·38	8	2·29	2·55	8	4·33	3·55	8	1·72	1·78
5	7·59	−7·38	3	3·41	−3·22	10	1·08	−1·09	9	2·00	−1·04			
7	4·00	4·42	5	2·45	−3·23				10	2·09	−2·09	$\bar{9}$.0.1	0·73	0·98
11	1·59	−1·66	6	2·58	−3·14	$\bar{2}$.0.1	13·08	16·83	11	1·57	−1·80	2	1·27	−1·36
			7	1·77	2·34	2	6·33	−4·43				3	3·05	−3·19
2.0.1	4·19	3·61	8	1·91	2·35	3	16·60	−16·13	$\bar{5}$.0.1	8·25	−8·07	5	2·37	2·65
3	2·42	−1·75				4	2·38	3·70	2	5·03	−4·65	6	1·35	0·63
4	12·84	−12·65	6.0.1	3·76	3·47	6	2·35	−3·58	4	4·36	−4·70	$\bar{1}\bar{0}$.0.1	1·10	−1·05
5	3·21	−2·86	4	2·30	−2·13	7	1·84	1·74	6	7·19	6·98	3	1·36	−1·03
6	3·09	3·86	5	4·06	−4·14	8	6·31	7·19	7	3·79	2·30	4	0·84	−0·92

0*kl*	F_o	A_c	B_c	$\|F_c\|$	0*kl*	F_o	A_c	B_c	$\|F_c\|$	0*kl*	F_o	A_c	B_c	$\|F_c\|$
0.2.0	12·75	13·47	−3·43	13·90	7	5·75	4·23	−3·19	5·30	7	1·82	0·71	−1·55	1·70
4	6·11	0·65	−5·61	5·65	8	2·61	−1·16	−1·33	1·76	8	1·96	−1·87	−1·06	2·15
6	4·07	3·82	0·79	3·90	9	1·14	−1·09	0·03	1·09	9	1·58	−1·26	−0·65	1·42
0.1.1	12·71	15·37	4·32	15·97	0.3.1	9·40	5·49	−7·31	9·13	0.5.1	4·55	−2·26	−3·14	3·87
2	28·37	−6·29	26·41	27·15	2	7·90	6·84	0·86	6·89	2	2·95	3·00	0·44	3·04
3	10·02	−7·88	7·28	10·73	3	4·17	3·48	−1·49	3·79	3	2·22	2·36	−0·28	2·38
4	7·92	5·17	−7·97	9·51	4	3·59	0·03	−4·15	4·15	4	2·18	−1·18	−1·50	1·90
5	7·51	−0·28	−7·47	7·48	5	5·45	−4·85	−0·20	4·86	5	1·74	−1·52	0·40	1·57
6	4·47	−3·47	0·67	3·53	6	6·97	−3·48	6·31	7·20	6	2·72	0·32	2·87	2·88
7	3·05	0·12	−3·27	3·27	7	1·23	−0·60	0·08	0·60					
8	1·51	1·21	−1·06	1·60	8	1·66	0·77	−2·26	2·39	0.6.1	1·96	−1·50	1·11	1·86
9	4·62	0·78	4·11	4·18	9	1·84	1·30	1·39	1·90	2	2·70	−3·07	−0·37	3·09
10	1·37	0·75	1·26	1·47	10	1·48	0·95	0·03	0·95	3	2·42	2·28	−0·81	2·42
										4	2·02	2·11	−0·49	2·17
0.2.1	4·88	−2·83	−2·41	3·72	0.4.1	4·94	−3·42	−3·28	4·74	5	1·37	−1·37	−0·43	1·43
2	5·69	−5·75	−0·67	5·79	2	1·87	−2·07	−0·72	2·20					
3	5·11	−0·26	4·25	4·26	3	4·31	2·43	3·86	4·56	0.7.1	1·24	−0·54	−1·21	1·32
4	5·03	1·64	3·53	3·90	4	6·75	4·13	4·58	6·17	2	1·19	−1·34	0·45	1·42
5	2·06	−1·94	1·24	2·31	5	1·85	0·63	1·12	1·29	3	1·19	−1·24	0·19	1·26
6	1·13	−0·10	0·91	0·91	6	1·06	−0·98	−0·69	1·20					

0*kl* projections, respectively. The molecule which is drawn in corresponds to the co-ordinates listed in Table 1. Fig. 2 shows the numbering of the atoms, the bond lengths and the bond angles. The whole molecule is planar within the limits of experimental

[3] Berghuis, Haanappel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.
[4] Tomiie and Stam, *Acta Cryst.*, 1958, **11**, 126.

error. The bond lengths and angles in general agree well with the expected values.[5] There are, however, some considerable differences between the present lengths and those found for the parent benzothiazoline-2-thione.[6] These differences occur round the nitrogen atom and lead to what appear to be more reasonable lengths and angles in the five-membered ring. The present results are not in accord with the curve relating C–S and C–N bond lengths in molecules of this type.[7] It is doubtful, however, whether the

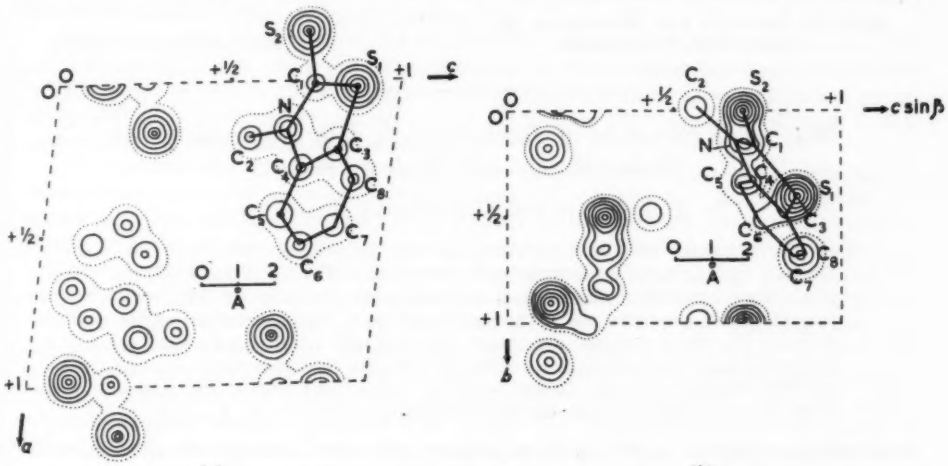


FIG. 1. (*a*) Projection of the contents of the unit cell down [*b*]. (*b*) Projection of the contents of the unit cell down [*a*]. (The contours are drawn at equal arbitrary intervals with some of the higher contours in the sulphur atoms omitted.

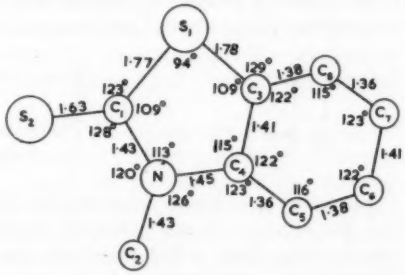


FIG. 2. The numbering of the atoms, the bond lengths, and the interatomic angles.

proposed relationship could have a very wide validity, particularly as it ignores the accurate refinement of thiourea by Kunchur and Truter.[8] There will clearly be some connection between the lengths of the C–N and C–S bonds, but several factors will probably play a part. The most important influence is whether the carbon atom $C_{(1)}$ is attached to one or to two nitrogen atoms, but even this can be affected if the nitrogen atoms are involved in the formation of a ring. There appear to be at present too few structure determinations to enable the effect of the different factors to be sorted out.

One strange similarity between the results of the present work and those for benzothiazoline-2-thione [6] is the distortion of the benzene ring. The difference between

[5] "Tables of Interatomic Distances," *Chem. Soc. Special Publ.*, No. 11.
[6] Tashpulatov, Zvonkova, and Zhdanov, *Kristallographiya*, 1957, **2**, 33.
[7] Zvonkova, Astakhova, and Glushkova, *Kristallographiya*, 1960, **5**, 547.
[8] Kunchur and Truter, *J.*, 1958, 2551.

dimensions of the benzene ring shown in Fig. 2 and a regular hexagon are probably within the limits of experimental error, but the results of the two analyses agree so well in this respect that it is tempting to believe that the distortion is real.

The intermolecular distances are normal, and there are no close approaches.

I thank Dr. R. A. Baxter and K. N. Ayad of Monsanto Chemicals Ltd., Ruabon, for suggesting this problem and for supplying the samples.

MONSANTO RESEARCH S.A., BINZSTRASSE 39,
ZURICH 3/45, SWITZERLAND.

[*Received, April 17th*, 1961.]

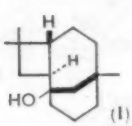
---

863. *The Structure of Isoclovene: X-Ray Analysis of the Hydrochloride and Hydrobromide.*

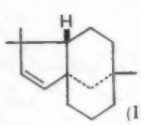
By J. S. CLUNIE and J. MONTEATH ROBERTSON.

The structure and stereochemistry of the tricyclic sesquiterpene isoclovene, $C_{15}H_{24}$, have been completely determined (IV) by *X*-ray analysis of the hydrochloride. The crystals are monoclinic, space group $P2_1$, with two molecules per unit cell. The ambiguity of a false symmetry centre between the phase determining atoms was gradually overcome by the use of three-dimensional methods. In the final results the discrepancy *R* over the 973 observed structure factors is 12·5%. The bond lengths and angles (Figs. 3 and 4) have average standard deviations of about 0·04 Å and 2°.

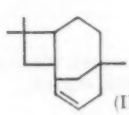
ISOCLOVENE, a tricyclic sesquiterpene of hitherto virtually unknown constitution, was first isolated by Henderson, McCrone, and Robertson [1] from the reaction mixture produced by treating β-caryophyllene alcohol (caryolan-1-ol) with phosphorus pentoxide. The other main product was believed at that time to be clovene. Subsequent chemical work,[2] when coupled with the results of Robertson and Todd's *X*-ray crystallographic analysis of the halides of β-caryophyllene alcohol,[3] has enabled structures (I) and (II) to be ascribed to β-caryophyllene alcohol and clovene, respectively.

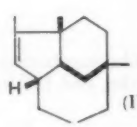


(I)



(II)


(III)



(IV)

Lutz and Reid [4] reinvestigated the dehydration of β-caryophyllene alcohol and showed that the mixture of oils obtained consisted of isoclovene and, not clovene, but a new isomer which they called pseudoclovene and for which they proposed structure (III). Although the latter workers do not appear to have studied isoclovene in any great detail, further investigations have been carried out by Money [5] who, on the basis of the infrared spectrum of isoclovene (peaks at 795s and 840m $cm.^{-1}$), inferred that the known ethylenic linkage was secondary-tertiary. In addition, Kuhn–Roth oxidation showed that the molecule contained three methyl groups.

The constitution of isoclovene, however, and its relation to clovene and pseudoclovene have remained obscure and further chemical work is rendered difficult by the ease with which unexpected molecular transformations occur in this series. On the other hand, isoclovene is characterised by a beautifully crystalline hydrochloride and hydrobromide

[1] Henderson, McCrone, and Robertson, *J.*, 1929, 1368.
[2] Barton, Bruun, and Lindsey, *J.*, 1952, 2210; Aebi, Barton, and Lindsey, *J.*, 1953, 3124.
[3] Robertson and Todd, *Chem. and Ind.*, 1953, 437; *J.*, 1955, 1254.
[4] Lutz and Reid, *J.*, 1954, 2265.
[5] Money, B.Sc. Thesis, Glasgow, 1957.

from which the pure hydrocarbon can be regenerated.[1] An *X*-ray investigation of these crystals was therefore undertaken, and from the results of this study, which are described below, the structure and stereochemistry of isoclovene can now be given unambiguously as (IV). The mechanism of the conversion of the alcohol (I) into isoclovene (IV) represents an unusual and difficult problem which cannot be completely solved on the basis of the known chemical facts. Some possible routes have already been discussed by Professor Barton in terms of carbonium-ion mechanism.[6]

Our *X*-ray work commenced with a study of the isomorphous isoclovene hydrochloride and hydrobromide, but owing to lack of resolution in the two-dimensional projections and to the complications of the isomorphous substitution method[7] in a non-centric space group ($P2_1$) this work was later abandoned in favour of a three-dimensional study of the hydrochloride by the heavy-atom method.[8]

The fundamental difficulty of a false symmetry centre between the two phase-determining atoms was, of course, again encountered. However, a selection of possible atomic sites was obtained by direct triple Fourier synthesis based solely on the chlorine phases and also by the application of superposition methods[9] to sharpened Patterson syntheses. At this stage a consideration of cell dimensions and van der Waals distances enabled the regions probably occupied by the two molecules to be delineated. A judicious selection of the more prominent peaks from what appeared to be one molecular site, and the gradual incorporation of these atoms into the phasing calculations, enabled the troublesome pseudo-symmetry to be overcome in the later electron-density distributions.

The refinement of the structure then proceeded by standard methods. Seven successive three-dimensional Fourier syntheses were carried out, during which the discrepancy R dropped from 47·4% to 20·4%. This was followed by twelve cycles of least-squares refinement, during which R decreased further to a final value of 12·5% over the 973 observed structure factors (Table 10). The course of the analysis is summarised in Table 2.

The final electron density distribution over one molecule is shown in Fig. 1. In this view along the b axis the ring systems are not clearly visible, but a roughly perspective drawing indicating the stereochemistry, and also the numbering system used in the later Tables, is given in Fig. 2. The molecular dimensions and estimated standard deviations (which average about 0·04 Å and 2°) are given in detail in Tables 6 and 7 but are summarised in Figs. 3 and 4.

The molecule is a very compact structure, consisting of a five-membered, a six-membered, and a seven-membered ring fused together, each ring retaining its preferred conformation. The five-membered ring is hinge-shaped, the six-membered ring has the chair conformation; the seven-membered ring is also in chair form but obviously distorted because all the angles are consistently greater than tetrahedral, the mean value being 116·5° (Fig. 4). This ring may be described as somewhat flattened, a situation probably due to steric repulsion as well as to ring strain. The increase in bond angles may be compared with those observed in cyclononylamine hydrobromide[10] and in 1,6-*trans*-diaminocyclodecane dihydrochloride[11] where similar large values for the ring angles have been found. In isoclovene, however, the fusion with neighbouring rings will cause additional strain. For example, in an ideal structure the non-bonded distance C(6) · · · C(10) would be only about 2·6 Å, whereas the distance found is 3·38 Å (Table 8).

The five-membered and six-membered rings are *cis*-fused, as are the five-membered and seven-membered rings. The six-membered and seven-membered rings are linked by a methylene bridge *cis* relative to C(14) and chlorine. The average carbon–carbon

[6] Clunie and Robertson, *Proc. Chem. Soc.*, 1960, 82.
[7] Robertson, *J.*, 1936, 1195; Bokhoven, Schoone, and Bijvoet, *Acta Cryst.*, 1951, **4**, 275.
[8] Robertson and Woodward, *J.*, 1937, 219; 1940, 36.
[9] Buerger, *Acta Cryst.*, 1951, **4**, 531.
[10] Bryan and Dunitz, *Helv. Chim. Acta*, 1960, **43**, 3.
[11] Huber-Buser and Dunitz, *Helv. Chim. Acta*, 1960, **43**, 760.

bond distance is 1·55 Å, with a maximum spread of 0·05 Å (average standard deviation, 0·04 Å). The quasi-axial carbon–chlorine bond of 1·86 Å can perhaps be considered as significantly longer than the expected value of 1·78 Å obtained from a consideration of atomic radii. Values as high as 1·85 Å and 1·84 Å for equatorial carbon–chlorine bonds in pentachlorocyclohexene have been reported by Pasternak.[12] For an axial carbon–chlorine bond in 1,2,3,4-tetrachloro-1,2,3,4-tetrahydronaphthalene a value of 1·81 Å has

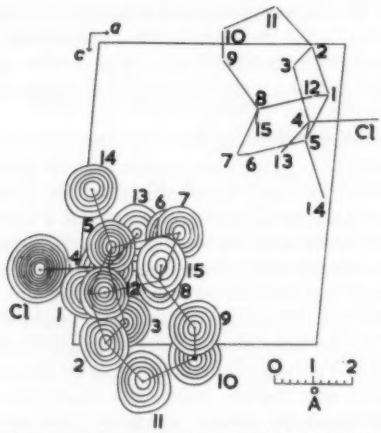


FIG. 1. Final electron-density distribution as superimposed contour sections drawn parallel to (010). Scale, carbon 1 eÅ^{-3}, chlorine 2 eÅ^{-3} per line. Atoms are drawn on section levels instead of accurately through atomic centres.

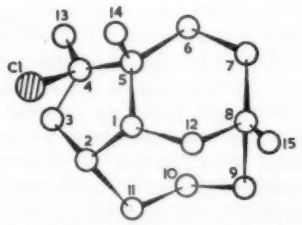


FIG. 2. Stereochemistry of isoclovene hydrochloride.

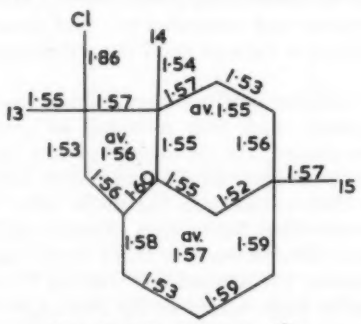


FIG. 3. Bond lengths (Å).

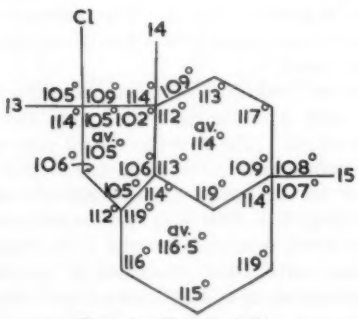


FIG. 4. Bond angles.

been cited.[13] The bond lengthening found in the present case may be simply a steric effect due to the proximity of two methyl and one methylene groups.

EXPERIMENTAL

In an attempt to employ the isomorphous substitution method fairly extensive measurements were made on isoclovene hydrobromide, including structure factor determinations for the three axial zones. As this work was later abandoned in favour of a three-dimensional

[12] Pasternak, *Acta Cryst.*, 1951, **4**, 316.
[13] Lasheen, *Acta Cryst.*, 1952, **5**, 593.

study of isoclovene hydrochloride, only elementary crystal data for the hydrobromide are given here.

Crystal Data.—Isoclovene hydrobromide, $C_{15}H_{25}Br$; M, 285·3; m. p. 74°; d, calc. 1·330, found 1·323 (flotation, zinc chloride solution). Monoclinic, $a = 6·48 \pm 0·01$, $b = 13·81 \pm 0·04$, $c = 7·96 \pm 0·01$ Å, $\beta = 91·9°$. Absent spectra, $(0k0)$ when k is odd. Space group, $P2_1$ (C_2^2) or $P2_1/m$ (C_{2h}^2). $P2_1/m$ must be rejected because the compound is optically active. Two molecules per unit cell. Volume of the unit cell = 712 Å^3. Absorption coefficient for X-rays, ($\lambda = 1·542$ Å) $\mu = 38·6$ cm.$^{-1}$. Total number of electrons per unit cell = $F(000) = 300$.

Small but well-formed prismatic needles elongated along a were obtained by slow crystallisation from acetone solutions. From two-dimensional Patterson and Fourier syntheses of the structure factors obtained from the axial zones, the following co-ordinates were obtained for bromine:

$$x/a = 0·177,\ y/b = 0·250,\ z/c = 0·242.$$

Isoclovene hydrochloride, $C_{15}H_{25}Cl$; M, 240·8; m. p. 87°; d, calc. 1·152, found 1·151 (flotation, zinc chloride solution). Monoclinic, $a = 6·35 \pm 0·01$, $b = 13·91 \pm 0·04$, $c = 7·89 \pm 0·02$ Å, $\beta = 95·3°$. Absent spectra, $(0k0)$ when k is odd. Space group, $P2_1$ (C_2^2) or $P2_1/m$ (C_{2h}^2). $P2_1/m$ must be rejected because the compound is optically active. Two molecules per unit cell. Volume of the unit cell = 694 Å^3. Absorption coefficient for X-rays ($\lambda = 1·542$ Å) $\mu = 22·2$ cm.$^{-1}$. Total number of electrons per unit cell = $F(000) = 264$. Crystal habit is similar to that of the hydrobromide.

Experimental Measurements.—Intensities were estimated visually from equi-inclination Weissenberg photographs taken with Cu-$K\alpha$ radiation. The layer lines surveyed and the dimensions of the crystal specimens are given in Table 1. As the cross-sections were small and nearly square no attempt was made to apply systematic absorption corrections.

TABLE 1.

Reflections surveyed.

Layer lines	Crystal cross section × length along rotation axis
$(0kl)$ — $(5kl)$	0·2 × 0·2 × 0·4 mm.^{3}
$(h0l)$	0·4 × 0·3 × 0·15 mm.^{3}
$(hk0)$ — $(hk4)$	0·25 × 0·3 × 0·2 mm.^{3}

Each reflection was estimated at least twice by using a different step wedge before the averaging process was performed. In all 1485 reflections were measured out of a possible 2725 (54·5%) and this yielded a total of 973 independent structure factors (Table 10), after the usual Lorentz, polarisation, and rotation correction factors had been applied. The absolute

TABLE 2.

Course of analysis.

Operation	Data used				R (%)	$\Sigma w\Delta^2$
3D Patterson function	973 F_o				—	—
3D minimum function	973 F_o				—	—
1st 3D F_o synthesis	Cl	885 F_o			47·4	—
2nd ,, ,,	Cl + 7C	614 F_o			40·2	—
3rd ,, ,,	Cl + 11C	776 F_o			38·7	—
4th ,, ,,	Cl + 13C	788 F_o			33·8	—
5th ,, ,,	Cl + 15C	882 F_o			27·9	—
6th ,, ,,	Cl + 15C	973 F_o			23·4	—
7th ,, ,,	Cl + 15C	973 F_o			20·4	—
1st least-squares cycle	Isotropic temp. factors			600 F_o	18·9	—
2nd ,, ,,	,,	,,	,,	600 F_o	16·4	—
3rd ,, ,,	,,	,,	,,	600 F_o	15·3	—
4th ,, ,,	,,	,,	,,	800 F_o	16·7	—
5th ,, ,,	Anisotropic temp. factors			973 F_o	15·6	259
6th ,, ,,	,,	,,	,,	,,	14·6	221
7th ,, ,,	,,	,,	,,	,,	13·7	209
8th ,, ,,	,,	,,	,,	,,	13·3	194
9th ,, ,,	,,	,,	,,	,, H atoms	13·0	191
10th ,, ,,	,,	,,	,,	,, ,,	12·9	185
11th ,, ,,	,,	,,	,,	,, ,,	12·6	179
12th ,, ,,	,,	,,	,,	,, ,,	12·5	179

TABLE 3.

Atomic co-ordinates and anisotropic temperature factors.

Atom	x/a	y/b	z/c	β_{11}	β_{22}	β_{33}	β_{23}	β_{31}	β_{12}
C(1)	−0·0440	−0·0470	0·1723	0·0326	0·0069	0·0222	−0·0043	0·0174	−0·0053
C(2)	−0·1275	−0·1055	0·0074	0·0424	0·0097	0·0261	0·0002	0·0306	0·0063
C(3)	−0·2027	−0·2045	0·0762	0·0394	0·0064	0·0279	−0·0010	−0·0011	0·0009
C(4)	−0·1137	−0·2110	0·2596	0·0406	0·0062	0·0255	−0·0009	−0·0007	0·0002
C(5)	−0·1179	−0·1048	0·3267	0·0304	0·0075	0·0221	0·0003	0·0094	0·0103
C(6)	−0·3516	−0·0806	0·3671	0·0200	0·0107	0·0254	0·0082	0·0031	−0·0036
C(7)	−0·3972	0·0274	0·3705	0·0407	0·0088	0·0247	0·0007	0·0093	0·0071
C(8)	−0·3316	0·0869	0·2131	0·0416	0·0069	0·0289	−0·0007	0·0198	−0·0021
C(9)	−0·4947	0·0734	0·0553	0·0333	0·0092	0·0309	0·0047	0·0018	−0·0073
C(10) ...	−0·5039	−0·0274	−0·0402	0·0387	0·0085	0·0225	−0·0048	−0·0050	0·0002
C(11) ...	−0·2980	−0·0578	−0·1193	0·0438	0·0099	0·0219	0·0040	−0·0054	−0·0031
C(12) ...	−0·1069	0·0607	0·1744	0·0331	0·0067	0·0255	−0·0011	0·0099	−0·0025
C(13) ...	−0·2208	−0·2893	0·3659	0·0514	0·0086	0·0329	0·0095	−0·0101	−0·0036
C(14) ...	0·0228	−0·0878	0·4887	0·0342	0·0102	0·0267	0·0006	−0·0119	−0·0017
C(15) ...	−0·3345	0·1960	0·2633	0·0615	0·0084	0·0884	−0·0027	0·0060	−0·0019
Cl	0·1650	−0·2512	0·2499	0·0341	0·0087	0·0347	−0·0043	0·0049	0·0076

TABLE 4.

Approximate hydrogen atom co-ordinates.

Atom no.	x/a	y/b	z/c	Atom no.	x/a	y/b	z/c
H(1)	0·116	−0·013	0·164	H(11′)	−0·252	−0·130	−0·154
H(2)	−0·030	−0·058	−0·069	H(12)	−0·153	0·109	0·049
H(3)	−0·140	−0·269	−0·001	H(12′)	0·022	0·105	0·226
H(3′)	−0·352	−0·244	0·067	H(13)	−0·364	−0·248	0·347
H(6)	−0·448	−0·133	0·295	H(13′)	−0·159	−0·361	0·350
H(6′)	−0·345	−0·113	0·492	H(13″)	−0·162	−0·276	0·497
H(7)	−0·530	0·058	0·441	H(14)	−0·119	−0·074	0·560
H(7′)	−0·288	0·067	0·449	H(14′)	−0·030	−0·138	0·586
H(9)	−0·438	0·001	−0·049	H(14″)	0·132	−0·055	0·492
H(9′)	0·391	0·025	0·100	H(15)	−0·335	0·241	0·150
H(10)	0·362	−0·073	−0·077	H(15′)	−0·474	0·218	0·333
H(10′)	−0·464	−0·099	0·087	H(15″)	−0·200	0·208	0·345
H(11)	−0·348	−0·018	−0·228				

TABLE 5.

Standard deviations in the positional co-ordinates.

Atom	$\sigma(x)$ (Å)	$\sigma(y)$ (Å)	$\sigma(z)$ (Å)	$\sigma(r)$ (Å) *	Atom	$\sigma(x)$ (Å)	$\sigma(y)$ (Å)	$\sigma(z)$ (Å)	$\sigma(r)$ (Å) *
C(1)	0·012	0·012	0·012	0·023	C(9)	0·013	0·014	0·015	0·027
C(2)	0·012	0·013	0·015	0·027	C(10) ...	0·013	0·012	0·014	0·026
C(3)	0·013	0·014	0·013	0·027	C(11) ...	0·014	0·013	0·015	0·028
C(4)	0·013	0·013	0·013	0·026	C(12) ...	0·012	0·013	0·013	0·025
C(5)	0·011	0·012	0·012	0·023	C(13) ...	0·015	0·016	0·015	0·030
C(6)	0·010	0·013	0·015	0·026	C(14) ...	0·013	0·015	0·015	0·029
C(7)	0·013	0·013	0·014	0·027	C(15) ...	0·016	0·017	0·016	0·033
C(8)	0·012	0·013	0·013	0·025	Cl	0·003	0·004	0·005	0·008

* Factor of 2 included to allow for non-centrosymmetry.

TABLE 6.

Bond lengths (Å) with standard deviations.

C(1)–C(2) ..... 1·600 ± 0·036	C(4)–C(5) ..... 1·570 ± 0·035	C(8)–C(9) ..... 1·590 ± 0·037
C(1)–C(5) ..... 1·547 ± 0·033	C(4)–C(13) ... 1·550 ± 0·040	C(8)–C(12) ... 1·518 ± 0·036
C(1)–C(12) ... 1·550 ± 0·034	C(5)–C(6) ..... 1·568 ± 0·035	C(8)–C(15) ... 1·568 ± 0·041
C(2)–C(3) ..... 1·563 ± 0·038	C(5)–C(14) ... 1·540 ± 0·038	C(9)–C(10) ... 1·590 ± 0·038
C(2)–C(11) ... 1·583 ± 0·039	C(6)–C(7) ..... 1·531 ± 0·038	C(10)–C(11) ... 1·533 ± 0·039
C(3)–C(4) ..... 1·527 ± 0·037	C(7)–C(8) ..... 1·561 ± 0·037	C(4)–Cl ..... 1·860 ± 0·027

scale was obtained at first approximately and later more accurately by correlation with the calculated values. From a study of about 400 reflections observed more than once the mean standard deviation of the structure amplitudes was found to be about $\sigma|F_i| = 0{\cdot}09|F_i|$.

Analysis of the Structure.—Approximate halogen positions had already been obtained from

TABLE 7.

Bond angles with standard deviations.

C(2)–C(1)–C(5)	105·7° ± 1·9°	C(5)–C(4)–C(13)	117·7° ± 2·2°	C(7)–C(8)–C(9)	111·6° ± 2·1°
C(2)–C(1)–C(12)	113·9 ± 1·9	C(13)–C(4)–Cl	104·7 ± 1·8	C(7)–C(8)–C(12)	108·6 ± 2·1
C(5)–C(1)–C(12)	115·1 ± 1·9	C(1)–C(5)–C(4)	102·4 ± 1·9	C(7)–C(8)–C(15)	107·9 ± 2·2
C(1)–C(2)–C(3)	105·2 ± 2·0	C(1)–C(5)–C(6)	111·8 ± 1·9	C(9)–C(8)–C(12)	113·5 ± 2·1
C(1)–C(2)–C(11)	119·2 ± 2·1	C(1)–C(5)–C(14)	112·6 ± 2·0	C(9)–C(8)–C(15)	107·2 ± 2·1
C(3)–C(2)–C(11)	112·1 ± 2·1	C(4)–C(5)–C(14)	113·8 ± 2·0	C(15)–C(8)–C(12)	107·8 ± 2·2
C(2)–C(3)–C(4)	105·9 ± 2·1	C(6)–C(5)–C(4)	107·5 ± 1·9	C(8)–C(9)–C(10)	118·8 ± 2·1
C(3)–C(4)–C(5)	104·5 ± 2·0	C(6)–C(5)–C(14)	108·5 ± 2·0	C(9)–C(10)–C(11)	114·9 ± 2·2
C(3)–C(4)–C(13)	113·5 ± 2·2	C(5)–C(6)–C(7)	113·3 ± 2·1	C(2)–C(11)–C(10)	115·6 ± 2·2
C(3)–C(4)–Cl	106·9 ± 1·8	C(6)–C(7)–C(8)	116·7 ± 2·2	C(1)–C(12)–C(8)	118·7 ± 2·1
C(5)–C(4)–Cl	109·2 ± 1·6				

TABLE 8.

Some intramolecular non-bonded distances (Å).

C(1)...Cl	= 3·18	C(3)...C(10)	= 3·23	C(7)...C(14)	= 3·21
C(1)...C(13)	= 3·89	C(4)...C(14)	= 2·61	C(7)...C(10)	= 3·36
C(1)...C(7)	= 2·98	C(5)...Cl	= 2·80	C(8)...C(11)	= 3·31
C(1)...C(10)	= 3·31	C(5)...C(13)	= 2·67	C(9)...C(15)	= 2·54
C(2)...Cl	= 3·30	C(5)...C(11)	= 3·70	C(10)...C(12)	= 3·21
C(2)...C(13)	= 3·87	C(5)...C(8)	= 3·10	C(11)...C(12)	= 3·04
C(2)...C(14)	= 3·87	C(6)...C(12)	= 2·97	C(12)...C(15)	= 2·49
C(2)...C(9)	= 3·44	C(6)...C(10)	= 3·38	C(12)...C(14)	= 3·30
C(3)...Cl	= 2·73	C(6)...C(14)	= 2·52	C(13)...C(14)	= 3·32
C(3)...C(13)	= 2·57	C(6)...C(13)	= 3·02	C(13)...Cl	= 2·71
C(3)...C(14)	= 3·84	C(7)...C(15)	= 2·53	C(14)...Cl	= 3·11

TABLE 9.

Some intermolecular distances (Å).

$C(1)...C(9_I)$	3·856 ± 0·036	$C(14)...C(11_{II})$	3·880 ± 0·041
$C(1)...C(10_I)$	3·495 ± 0·035	$C(15)...Cl_{III}$	3·960 ± 0·034
$Cl...C(6_I)$	3·922 ± 0·027	$C(9)...C(3_{IV})$	3·734 ± 0·038
$Cl...C(13_I)$	3·959 ± 0·031		

(The subscripts refer to the following positions: I $1 + x, y, z$. II $x, y, 1 + z$. III $1 - x, \frac{1}{2} + y, \bar{z}$. IV $\bar{x}, \frac{1}{2} + y, \bar{z}$.)

our preliminary two-dimensional work on isoclovene hydrobromide. For the hydrochloride a three-dimensional sharpened Patterson function incorporating all the observed structure factors was prepared in sections parallel to the *b* axis. A completely resolved chlorine–chlorine vector peak was not at first obtained, but by the application of superposition methods [9] unambiguous co-ordinates were finally derived, and refined by later Fourier syntheses.

The fundamental difficulty of the analysis, in space group $P2_1$, is, of course, due to the fact that the two phase-determining chlorine atoms are related by a two-fold screw axis and false symmetry is thereby introduced to the electron-density distribution derived from these phases. This difficulty was further aggravated in the present case by the discovery that the *z*-co-ordinate of the chlorine atom was extremely close to the special value of 0·250, with the result that the chlorine atoms made almost zero contribution to certain sets of reflections, with the consequent introduction of additional spurious symmetry in certain projections.

No very direct method is known for overcoming these difficulties and recourse must be had to a knowledge of what is chemically reasonable in attempting to interpret the results. By using almost the full three-dimensional data, a minimum function was prepared and also a Fourier synthesis based solely on the chlorine phases. From a careful comparison of these two functions the peaks that were most likely to represent atomic sites were selected. At this stage each peak was duplicated by the false symmetry, but the selection of true sites was helped by the apparently compact nature of the molecules and the comparatively large gaps between them (compare Figs. 5 and 6). At first only seven atoms were included in the phasing calculations in addition to chlorine, but a notable decrease in the discrepancy factor *R* indicated that a substantially correct choice had been made. In later stages of the work many false peaks still remained, but these were generally of smaller height and more irregular in outline than the peaks representing genuine atoms. The five-membered and six-membered rings first clearly emerged as definite molecular features. It at first appeared possible that the remaining ring

might also be six-membered, but the discovery of atom C(10) in a mirror image position to C(9) across the pseudo-symmetry centre at ($\frac{1}{2}$00) established the true nature of this ring and effectively completed the structure determination.

The course of the analysis is summarised in Table 2. For the 6th and 7th F_o synthesis the "*n* shift" rule of Shoemaker and others [14] with $n = 1{\cdot}6$ was applied. After the 7th F_o synthesis, refinement was continued by the method of least squares, only the diagonal elements of the matrix of normal equations being used. The isotropic temperature factors used in the initial cycles were $B = 3{\cdot}5$ Å^2 for carbon and $B = 4{\cdot}4$ Å^2 for chlorine, with the scattering factors of Berghuis and others [15] for carbon, and of James and Brindley [16] for chlorine. In the last four cycles hydrogen contributions were included in the structure factors calculated

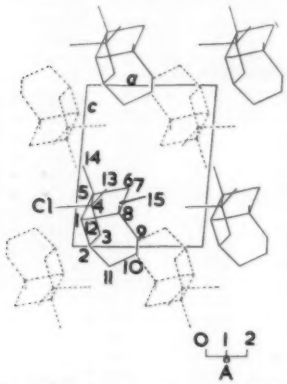


FIG. 5. The structure projected on (010).

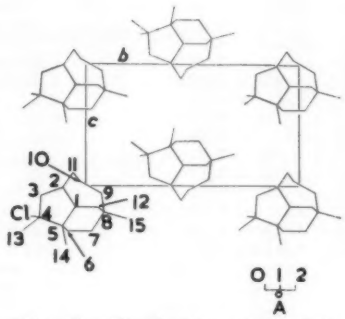


FIG. 6. The structure projected on (100).

by the least-squares programme, but the hydrogen co-ordinates were not refined. They were assumed to lie in the geometrically required positions, with a carbon–hydrogen bond length of 1·05 Å. The methyl-hydrogen atoms were assumed to lie in positions staggered with respect to the substituents on the adjacent carbon atoms.

The weighting system used for the least-squares analysis was as follows:

$$\sqrt{w} = 1 \text{ if } |F_o| \leqslant 8|F_{\text{min.}}|$$

$$\sqrt{w} = \frac{8|F_{\text{min.}}|}{|F_o|} \text{ if } |F_o| > 8|F_{\text{min.}}|$$

The value of $\sum w\Delta^2$, the quantity minimised in the least-squares process, decreased steadily to 185 in the 10th cycle and then remained almost constant. Together with the almost constant value of R during the last few cycles, this indicated that refinement within the scope of the present data and the methods used was complete.

The final co-ordinates and anisotropic temperature factors are given in Tables 3 and 4. The thermal parameters listed are derived from the 12th least squares cycle, by using the programme of Rollett [17] and the form

$$T = 2^{-(\beta_{11}h^2 + \beta_{12}k^2 + \beta_{33}l^2 + \beta_{23}kl + \beta_{31}lh + \beta_{12}hk)}$$

where $\beta_{11} = 1{\cdot}4427B_{11}$, etc. Equivalent isotropic temperature factors deduced by the method of Rossmann and others [18] are $B = 4{\cdot}4$ Å^2 for the average carbon atom and $B = 4{\cdot}45$ Å for the chlorine atom.

[14] Shoemaker, Donohue, Schomaker, and Corey, *J. Amer. Chem. Soc.*, 1950, **72**, 2328.
[15] Berghuis, Haanappel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.
[16] James and Brindley, *Phil. Mag.*, 1932, **12**, 81.
[17] Rollett, "Computing Methods and the Phase Problem in *X*-Ray Crystal Analysis," ed. Pepinsky, Robertson, and Speakman, Pergamon Press, Oxford, 1961, p. 87.
[18] Rossmann, Jacobson, Hirshfeld, and Lipscomb, *Acta Cryst.*, 1959, **12**, 530.

XUM

TABLE 10.

Observed and calculated structure factors.

The standard deviations in the positional co-ordinates given in Table 5 were calculated directly from the least-squares output by standard procedures. The molecular dimensions, also with their appropriate standard deviations, are given in Tables 6 and 7, with some non-bonded intramolecular distances in Table 8.

The packing of the molecules in the crystal can only be fully studied by means of models, but the projections of the structure shown in Figs. 5 and 6 indicate the general arrangement. No unusual approach distances occur, the shortest being 3·5 Å between carbon atoms of adjoining molecules. A sample of the intermolecular distances is given in Table 9.

We thank Dr. G. A. Sim for helpful advice on many points during this work. One of us (J. S. C.) is indebted to the Carnegie Trust for a scholarship. The extensive numerical calculations were nearly all carried out on the Glasgow University Deuce computer.

CHEMISTRY DEPARTMENT, UNIVERSITY OF GLASGOW. [*Received, April 19th,* 1961.]

---

864. *Organic Peroxides. Part X.* The Autoxidation of Ethyl Chaulmoograte: the Course and Stereochemistry of Homolytic Autoxidation.*

By ALWYN G. DAVIES and J. E. PACKER.

The infrared spectrum and chemical properties of the autoxidation product of (−)-ethyl chaulmoograte (III) show it to be an unsaturated hydroperoxide, and not the " oxoxide " (IV) as has been suggested.

The hydroperoxide is essentially optically inactive. The unsaturated alcohol which is formed by reduction of the hydroperoxide with borohydride has been partially resolved, and then hydrogenated to an optically inactive saturated alcohol. It is concluded that the hydroperoxide has at least principally the structure (±)-(V). This appears to be the first demonstration that homolytic autoxidation proceeds with racemisation.

IT has often been suggested that there might exist a family of isolable compounds of the structure (I), isomeric with structure (II) which is commonly accepted for the organic peroxides. These compounds (I) have been called oxoxides,[1] because of their analogy with the sulphoxides and amine oxides These suggestions, however, have not withstood examination, and although the existence of the compounds (I) remains a formal possibility, no example has yet been firmly established.

(I) $R_2O\rightarrow O$ RO·OR (II)

The case has recently been reopened by Bernard [2] who studied the polarographic behaviour of a number of peroxides in buffered 0·5N-aqueous potassium sulphate. One group of compounds (ammonium persulphate, peroxyacetic acid, peroxybenzoic acid, t-butyl peroxybenzoate, the peroxide of cyclohexanone, cumene peroxide, pinene peroxide, the peroxide of ether, and the peroxide of dioxan) showed a reduction wave at 0·0 v. These easily reduced peroxides were assigned the " true peroxide " structure (I). The second group (acetone peroxide, t-butyl hydroperoxide, ethyl hydroperoxide, dibutyl peroxide, the peroxide of acetaldehyde, and hydrogen peroxide) were reduced with more difficulty, at −0·3 to −1·1 v, and were regarded as having the so-called " hydroperoxide " structure (II).

These conclusions have been applied by Baranger and Maréchal [3] in their study of the

* Part IX, *J.*, 1958, 4637.

[1] Rieche, " Alkyl Peroxyde und Ozonide," Steinkopff, Dresden, 1931, pp. 97, 161.
[2] Bernard, *Compt. rend.*, 1953, **236**, 2412; *Ann. Chim.* (*France*), 1955, **10**, 315; *Parfumerie, Cosmet., Savon*, 1958, **1**, 467.
[3] Baranger, *J. Inter. Leprosy*, 1948, 49; Baranger and Maréchal, *Compt. rend.*, 1950, **231**, 661; *Bull. Soc. chim. France*, 1957, 782.

XUM

autoxidation of ethyl chaulmoograte (III).† They assigned to the product the structure (IV), and rejected the possibility that it might be an allylic hydroperoxide (*e.g.*, V) on the basis of the following evidence: (1) The uptake of oxygen was accompanied by an equivalent loss of unsaturation. (2) The product could not be acetylated (RO·OH ⟶ RO·OAc), nor could it be alkylated with xanthhydrol or triphenylmethanol (RO·OH ⟶ RO·OR'): the reaction with xanthhydrol gave only dixanthen-9-yl peroxide. (3) The polarographic behaviour of the peroxide was typical of Bernard's class of "true" peroxides (I).

We have therefore investigated the structure of the peroxide formed by the autoxidation of ethyl chaulmoograte, because it appeared to be the best authenticated example of a peroxide of the type (I).‡

Experimental

Unless otherwise stated, all optical rotations were measured for chloroform solutions.

Analysis.—Peroxides were analysed iodometrically in propan-2-ol solution. Olefinic double bonds were estimated (*a*) by quantitative hydrogenation over platinum oxide, the gas burette described in ref. 7 being modified and the sample added magnetically after the catalyst had been reduced, or (*b*) by Baranger and Maréchal's modification [8] of Hanus's method [4,8] (iodine bromide).

Gas–liquid chromatography of the ethyl chaulmoograte was carried out on a 4 mm. × 1 m. column of silicone grease E 301 on "Celite" at 230° with air (5 c.c./min.) as the carrier gas. We are very grateful to the Analytical Department of Imperial Chemical Industries Limited, Dyestuffs Division, for performing these analyses.

Preparation of Ethyl Chaulmoograte (III).—Ethyl chaulmoograte was obtained from chaulmoogra oil by the following procedure.[9]

Chaulmoogra oil (2 kg.) was saponified for 4 hr. with potassium hydroxide (1 kg.) in boiling ethanol (5 l.). From two reactions, 3·9 kg. of wet acid were obtained. This acid was boiled for 6 hr. in ethanol (4 l.) containing sulphuric acid (150 c.c.), giving 3·2 kg. of mixed ethyl esters. The esters were fractionally distilled at low pressure through a column 95 cm. × 18 mm. packed with Fenske glass helices. The progress of the fractionation was checked by gas–liquid chromatography of the distillate. Two principal fractions were collected: (*a*) crude ethyl hydnocarpate (1343 g.), b. p. 152—156°/*ca.* 0·4 mm., and (*b*) crude ethyl chaulmoograte (1450 g.), b. p. 164—175°/*ca.* 0·2 mm. Fraction (*b*) was saponified for 1 hr. with potassium hydroxide (140 g.) in boiling ethanol (1 l.), and the crude chaulmoogric acid was recrystallised once from ethanol–water (4 : 1 v/v) and twice from ethanol–pentane, giving chaulmoogric acid (432 g.), m. p. 69°, $[\alpha]_D$ +59·3°.

Chaulmoogric acid (300 g.) was heated under reflux in absolute ethanol (1·8 l.) containing concentrated hydrochloric acid (4 c.c.), yielding ethyl chaulmoograte (270 g.), b. p. 143—146°/0·01 mm., $[\alpha]_D$ +51·0° (Found: C, 77·4; H, 11·6. Calc. for $C_{20}H_{36}O_2$: C, 77·8; H, 11·8%). The gas–liquid chromatogram showed only one peak and demonstrated the absence of ethyl hydnocarpate. The infrared spectrum is shown in the Figure.

Ethyl 2',3'-Epoxychaulmoograte (VIII).—Ethyl chaulmoograte (3·91 g.) was mixed with peroxyoctanoic acid (2·13 g.) in benzene, the mixture becoming warm. After 15 hr. the solution was washed three times with ice-cold 10% sodium hydroxide solution and dried (Na_2SO_4). The benzene was removed and the residue was recrystallised from light petroleum at low temperature, giving *ethyl 2',3'-epoxychaulmoograte*, m. p. 30—33°, $[\alpha]_D$ +19·5° (Found:

† Baranger and Maréchal suggest that the antileprotic activity of ethyl chaulmoograte is due to the adventitious presence of a small amount of the peroxide formed by reaction with air.

‡ The "peroxide" formed from the reaction of fluorenone with hydrogen peroxide [4] is, in fact, a complex between the ketone and its *gem*-dihydroperoxide,[5] and not an oxoxide as is often supposed.[4,6]

[4] Wittig and Pieper, *Ber.*, 1940, **73**, 295.
[5] Criegee, Schnorrenberg, and Becke, *Annalen*, 1948, **565**, 7; Criegee, *Fortschr. chem. Forsch.*, 1950, **1**, 508.
[6] Syrkin and Moiseev, *Russ. Chem. Rev.*, 1960, **29**, 193 (esp. p. 197).
[7] Abraham and Davies, *J.*, 1959, 429.
[8] Norris and Buswell, *Ind. Eng. Chem., Analyt.*, 1943, **15**, 259.
[9] Cf. Gupta and Malkin, *J.*, 1952, 2405.

C, 73·3; H, 11·35. $C_{20}H_{34}O_3$ requires C, 74·0; H, 11·2%). The infrared spectrum is shown in the Figure.

Autoxidation of Ethyl Chaulmoograte.—Ethyl chaulmoograte (80 g.) was shaken under oxygen in a flask connected to a gas burette [7] by flexible tubing. The flask was contained in a large air-bath (a tea chest) kept at *ca.* 35° by a high-pressure mercury lamp, a tungsten-filament lamp, or a hot-plate. The rate of uptake of oxygen, and the nature of the product, were independent of the method of heating: the reactions were always preceded by an induction period and then appeared to be autocatalytic. The relation between the amount of oxygen absorbed (recorded on the gas burette) and the peroxide formed (measured iodometrically) is shown in Table 1.

TABLE 1.

Autoxidation of ethyl chaulmoograte.

O_2 absd. (mol.)	0	0·033	0·056	0·066	0·130
Peroxide formed (mol.)	0	0·033	0·053	0·057	0·099
$[\alpha]_D$ (found)	+51·0°	—	—	+47·9°	+45·6°
$[\alpha]_D$ (calc.[a])	+51·0°	—	—	+47·4°	+43·6°

[a] By assuming that the peroxide is inactive and has a simple dilution effect on the rotation of the ethyl chaulmoograte.

It will be seen that initially all the oxygen is taken up as peroxide but, as the reaction proceeds, some non-peroxide products are formed; if the peroxide is inactive, these impurities appear to be dextrorotatory. It was convenient to continue the oxidation for 12 hr., by which time about 5% of peroxide had been formed, with little or no non-peroxidic products.

Isolation of Ethyl 1′-Hydroperoxychaulmoograte (V).—Alumina was washed once with acetic acid and five times with light petroleum (b. p. 40—60°), and then packed wet into a column 30 × 4 cm. and washed with light petroleum until all the acetic acid was removed. Ethyl chaulmoograte (80 g.), autoxidised to the extent of 5%, in light petroleum (150 c.c.) was then added to the column and eluted with light petroleum.

The presence of the ester in the eluate was indicated by the formation of a translucent spot when a drop of the eluate was allowed to evaporate on filter paper. The peroxide was detected by spraying the paper with an acid ferrous thiocyanate reagent.[10] The peroxide was then eluted with ethanol, and the solvent removed, leaving the peroxide mixed with some aluminium acetate. This was extracted with light petroleum, the extract was washed and dried, and the solvent removed to constant weight, giving *ethyl 1′-hydroperoxychaulmoograte* as a colourless oil [Found: C, 70·8; H, 10·7; peroxidic O, 8·6%; *M* (by iodine bromide), 343, 345; *M* (by hydrogenation of C=C and O–O in a different specimen, see below), 354. $C_{20}H_{36}O_4$ requires C, 70·6; H, 10·7; peroxidic O, 9·4%; *M*, 340·5]. The infrared spectrum is shown in the Figure.

The relation between the purity and the optical rotatory power of specimens from different preparations was as follows (% peroxide; $[\alpha]_D$): 92%, 1·6°; 88%, 4·8°; 81%, 6·8°; 79%, 6·1°.

One preparation was further purified by partition between equal volumes of light petroleum (b. p. 40—60°) and ethanol–water (88 : 12 v/v) in a 25-tube countercurrent separator. The crude peroxide (0·70 g.), 76% pure, $[\alpha]_D$ +5·8° (in EtOH), gave, in tubes 1, 2, and 3 combined, 0·063 g. of peroxide 85% pure, $[\alpha]_D$ +0·8° (in EtOH); and, in tubes 7, 8, and 9 combined, 0·17 g. of peroxide, 75% pure, $[\alpha]_D$ +6·9° (in EtOH).

Ethyl 1′-(1,2-Dihydro-1-methyl-6,8-dinitroquinoline-2-peroxy)chaulmoograte [by Mr. R. J. STEVENS].—A solution of the hydroperoxide (0·7 g.) in ether was shaken for 2 min. with a solution of 2-ethoxy-1,2-dihydro-1-methyl-6,8-dinitroquinoline [11] (0·4 g.) in acetic acid. The product was twice recrystallised from light petroleum–ether, yielding the yellow *derivative*, m. p. 64·0—64·5° (Found: C, 62·6; H, 7·7; N, 7·3. $C_{30}H_{43}N_3O_8$ requires C, 62·8; H, 7·6; N, 7·3%).

Attempts to prepare the triphenylmethyl derivative (from triphenylmethyl chloride and pyridine) and the xanthen-9-yl derivative (from xanthhydrol in acetic acid) were not successful.

Ethyl 1′-Hydroxychaulmoograte (VI).—The hydroperoxide ($[\alpha]_D$ +6·15° and +4·76° in two experiments) in ten times its volume of ether was mixed with a solution of sodium borohydride in ethanol; the reaction was slightly exothermic. Next day the mixture was washed with acid, and the ethereal layer yielded impure ethyl 1′-hydroxychaulmoograte ($[\alpha]_D$ +5·94° and +4·22°, from the above two samples respectively) as an oil which solidified just below room temperature.

[10] Abraham, Davies, Llewellyn, and Thain, *Analyt. Chim. Acta*, 1957, **17**, 499.
[11] Rieche, Schmitz, and Dietrich, *Chem. Ber.*, 1959, **92**, 2239.

XUM

Sodium sulphite and triphenylphosphine were less satisfactory reducing agents.

Ethyl 2′,3′-Dihydro-1′-hydroxychaulmoograte (VII).—The unsaturated hydroperoxide (89% pure; 0·4232 g.) in ethanol was hydrogenated over platinum oxide at atmospheric pressure and room temperature during 1·5 hr.; 104% of the calculated volume of gas was absorbed (possible unsaturation in the 11% of impurity being ignored), and there was an obvious decrease in the rate of reaction after the reduction was half-complete. The solution was filtered and the alcohol removed under reduced pressure, yielding *ethyl 2′,3′-dihydro-1′-hydroxychaulmoograte* (from light petroleum), m. p. 33—35° (Found: C, 73·5; H, 11·6. $C_{20}H_{38}O_3$ requires C, 73·5; H, 11·7%). The ester was hydrolysed and the product was recrystallised from aqueous ethanol, giving *2′,3′-dihydro-1′-hydroxychaulmoogric acid*, m. p. 81·5° (Found: C, 72·8; H, 11·5. $C_{18}H_{34}O_3$ requires C, 72·5; H, 11·5%).

Infrared spectra of (a) ethyl chaulmoograte (III), (b) ethyl 1′-hydroperoxychaulmoograte (V), (c) (V) + ethyl 1′-deuteroperoxychaulmoograte, (d) ethyl 1′-hydroxychaulmoograte (VI), (e) ethyl 2′,3′-dihydro-1′-hydroxychaulmoograte (VII), and (f) ethyl 2′,3′-epoxychaulmoograte (VIII).

Hydrogenation of a sample of the hydroperoxy-ester (81% pure), $[\alpha]_D$ +6·8°, gave the crude product, $[\alpha]_D$ −4·0°.

A mixture of ethyl dihydrohydroxychaulmoograte (0·625 g.), phthalic anhydride (0·293 g.), pyridine (0·4 c.c.), and benzene (0·3 c.c.) was kept at 75° for 4·5 hr. The only acid product recovered was phthalic acid. Under the same conditions, cyclopentanol gave *cyclopentyl hydrogen phthalate* (from carbon disulphide–light petroleum), m. p. 61·0—61·5° (Found: C, 67·0; H, 6·2. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%).

Infrared Spectra.—The spectra shown in the Figure were recorded on a Grubb-Parsons model G.S.2A double-beam grating instrument.

Partial deuteration of the hydroperoxy-group was carried out as follows. Ethyl 1′-hydroperoxychaulmoograte (0·329 g.) was mixed with 99% D_2O (0·034 g.), and dioxan was added slowly to give a homogeneous solution. All volatile material was removed under reduced pressure and the product was thoroughly dried. The absorption at 2·90 μ (OH stretching) was found to have diminished and a new peak at 3·95 μ (OD stretching; cf. $Ph{\cdot}CMe_2{\cdot}O{\cdot}OD$ [12]) appeared. This trend was continued by a second similar treatment.

Resolution of 1′-Hydroxychaulmoogric Acid.—Crude ethyl 1′-hydroxychaulmoograte was heated under reflux for 1 hr. in ethanol containing a slight excess of concentrated aqueous

sodium hydroxide. The product was acidified at 0° with nitric acid, yielding 1′-hydroxychaulmoogric acid. It was slightly soluble in light petroleum and recrystallised from that solvent at −70°, but attempts to purify the acid at this stage were unsuccessful.

Equivalent amounts of the crude acid (4·5 g.), $[\alpha]_D$ +6·0°, and of brucine were dissolved in warm ethyl acetate. After some days at 2°, light buff crystals of the brucine salt had separated; these were filtered off and recrystallised from ethyl acetate. The brucine salt was decomposed with dilute acid and the optically active *1′-hydroxychaulmoogric acid* (0·4 g.) was extracted with ether and recovered, with m. p. 56—58°, $[\alpha]_D$ +24·1° (Found: C, 72·2; H, 10·8. $C_{18}H_{32}O_3$ requires C, 72·9; H, 10·9%). An equivalent rotation could be given by a mixture of inactive hydroxychaulmoogric acid (60%) and (+)-chaulmoogric acid (40%) (Calc. for this mixture: C, 74·6; H, 11·1%).

In a second experiment the crude acid, $[\alpha]_D$ +6·5° (9 g.), yielded (+)-1′-hydroxychaulmoogric acid, $[\alpha]_D$ +18·0°.

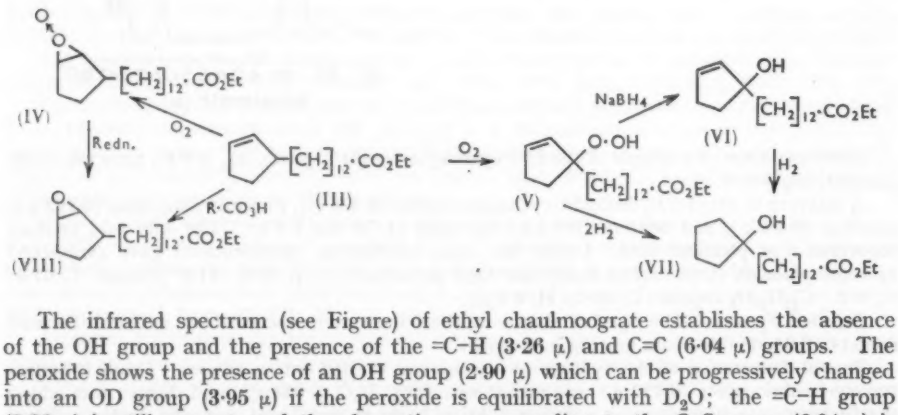
Hydrogenation of (+)-1′-Hydroxychaulmoogric Acid.—The (+)-acid (0·2143 g.), $[\alpha]_D$ +24·1°, in ethanol containing platinum oxide, absorbed 96% of the calculated volume of hydrogen, yielding inactive 2′,3′-dihydro-1′-hydroxychaulmoogric acid. This confirms the view that the reduction had not isolated merely the active impurity from the impure starting material, because the impurity (see above) gives a lævorotatory product on reduction.

In a second experiment the (+)-acid (0·2096 g.), $[\alpha]_D$ +18°, absorbed 103% of the calculated volume of hydrogen. The saturated hydroxy-acid which was formed was converted into the ethyl ester and thoroughly dried. The infrared spectrum, particularly the ratio of the heights of the peaks at 2·90 (OH) and 5·75 μ (C=O), confirmed the product as ethyl 2′,3′-dihydro-1′-hydroxychaulmoograte.

Discussion

The Nature of the Peroxide.—Ethyl chaulmoograte (III) was shaken at 35° under oxygen and the peroxide which was formed was periodically analysed iodometrically (Table 1). Up to about 5% autoxidation, essentially all the oxygen is absorbed to form titratable peroxide; further oxidation gives an appreciable amount of non-peroxidic material.

The peroxide was isolated in 92% purity by chromatography on acetic acid-washed alumina: the following evidence shows clearly that the product is a hydroperoxide, and does not have the structure (IV).



The infrared spectrum (see Figure) of ethyl chaulmoograte establishes the absence of the OH group and the presence of the =C–H (3·26 μ) and C=C (6·04 μ) groups. The peroxide shows the presence of an OH group (2·90 μ) which can be progressively changed into an OD group (3·95 μ) if the peroxide is equilibrated with D_2O; the =C–H group (3·26 μ) is still present, and the absorption corresponding to the C=C group (6·04 μ) is stronger than in ethyl chaulmoograte, implying that the double bond is now polarised by a neighbouring polar group. This spectrum is therefore that which would be predicted for a hydroperoxide such as (V) and is not compatible with the requirements of structure (IV) which should show the absence of the OH, =C–H, and C=C groups.

Further support for the hydroperoxide structure came unexpectedly from a study of the C=O absorption of the carboxylic ester group. Ethyl chaulmoograte and its non-peroxidic derivatives decribed below (see Figure) show the presence of this group by a single peak at 5·75 μ; in the hydroperoxy-ester, which we showed to be free from acid, this is accompanied by a slightly smaller peak at 5·82 μ. A similar doublet is obtained if t-butyl hydroperoxide is added to ethyl chaulmoograte and it appears to arise through association between the hydroperoxy- and the carbonyl-group, probably because of the powerful hydrogen-bonding power of the hydroperoxide. An analogous effect has been recorded in the infrared spectrum of acetic acid. At 60° the vapour shows the presence of two peaks at about 5·60 and 5·76 μ, ascribed to the monomer and dimer respectively; at 20° the amount of dimer and its corresponding peak increase in importance, and in the liquid phase, when the acid is fully associated, only one peak is observed, at about 5·83 μ.[13]

The peroxide was reduced with sodium borohydride: the only changes in the spectrum were the disappearance of the peak at 5·82 μ, referred to above, and a slight reduction in the intensity of the OH absorption, as would be expected [14] if a hydroperoxide were being reduced to the corresponding alcohol (*e.g.*, V ⟶ VI). If the peroxide had the structure (IV), the first reduction product might be expected to be the epoxide (VIII). This epoxide was therefore prepared by treating ethyl chaulmoograte with peroxyoctanoic acid, and its spectrum (see Figure) was found to differ from that of the reduced peroxide.

Baranger and Maréchal's strongest evidence for the structure (IV) was perhaps the fact that the autoxidation involved saturation of the 2′,3′-olefinic bond.[3] Using their analytical method (the reaction with iodine bromide) we find in contrast to their results, and in agreement with the infrared evidence described above, that the peroxide contained intact the carbon–carbon double bond. This was confirmed by quantitative hydrogenation of the peroxide; two mol. of hydrogen were absorbed to give a saturated alcohol (*e.g.*, V ⟶ VII) whose infrared spectrum (see Figure) now shows the absence of =C–H and C=C groups.

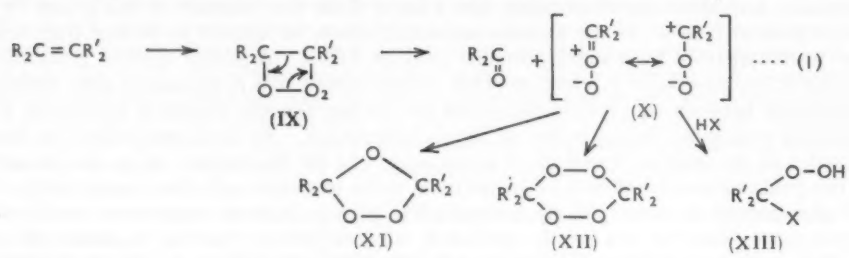
Rieche and his colleagues [11] have recently shown that characteristic derivatives of hydroperoxides can be obtained by causing them to react with 2-ethoxy-1,2-dihydro-1-methyl-6,8-dinitroquinoline, to give the corresponding 2-alkylperoxy-compounds. We have obtained this derivative of our autoxidation product, confirming again that it is a hydroperoxide.

We conclude therefore that the autoxidation product of ethyl chaulmoograte is a conventional unsaturated hydroperoxide, and that the oxoxide structure (IV) is not correct. Baranger and Maréchal [3] were probably misled because their experiments, particularly the analyses for unsaturation, were apparently carried out, not on the isolated peroxide, but on ethyl chaulmoograte which had been autoxidised to the extent of 22% (and, from our results, would contain an appreciable amount of by-products). They interpreted the fact that the reaction with xanthhydrol gave dixanthen-9-yl peroxide as supporting evidence for the structure (IV). We, on the other hand, regard it as support for an allylic hydroperoxide structure such as (V), which under acid conditions eliminates hydrogen peroxide which is then alkylated by the xanthhydrol; pinane hydroperoxide,[15] 3-methyl-1-phenylallyl hydroperoxide, and 1-methyl-3-phenylallyl hydroperoxide [16] react similarly with triphenylmethanol to give bis(triphenylmethyl) peroxide.

It is less easy to reinterpret Bernard's polarographic results; few of the compounds which he classified as " true peroxides " were isolated, their solubility in water would be very low, and most of the polarographic measurements were carried out on aqueous extracts of the autoxidised oils. Even if his results are accepted at their face value,

[13] Simon, Jentzsch, and Menzel, *Chem. Ber.*, 1959, **90**, 1023.
[14] Herman and Hofstader, *J. Chem. Phys.*, 1938, **6**, 534; Davies and Sutherland, *J. Chem. Phys.*, 1938, **6**, 755; Hartwell, Richards, and Thompson, *J.*, 1948, 1436.
[15] Williams and Mosher, *Analyt. Chem.*, 1955, **27**, 517; Khan, *J. Org. Chem.*, 1958, **23**, 606.
[15] M. H. Abraham, personal communication.
[16] Feld, *Chem. and Ind.*, 1959, 1600.

however, they would seem to be an inadequate foundation, without supporting evidence, for proposing the existence of a new class of compounds



We believe that there is still no established example of a stable oxoxide. The best evidence for the formation of this structure appears to be as an unisolated reactive intermediate in the ozonisation of olefins (eqn. 1).[17] The unstable "initial ozonide" * (IX) is assumed to break down to a carbonyl compound and oxoxide (X) which rapidly adds to the carbonyl compound, or to itself, or to a reagent HX, to give a peroxide (XI), (XII), or (XIII) of conventional structure.

The Position of the Hydroperoxy-group and the Stereochemistry of the Autoxidation.— The autoxidation of a hydrocarbon to an alkyl hydroperoxide is generally accepted to proceed by a free-radical chain mechanism (eqns. 2—4).

$$RH \longrightarrow R\cdot + [H\cdot] \quad \ldots\ldots\ldots\ldots (2)$$

$$R\cdot + O_2 \longrightarrow RO\cdot O\cdot \quad \ldots\ldots\ldots\ldots (3)$$

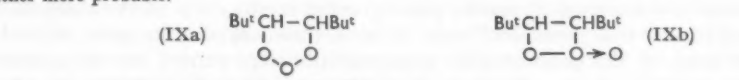
$$RO\cdot O\cdot + RH \longrightarrow RO\cdot OH + R\cdot \quad \ldots\ldots\ldots\ldots (4)$$

The reaction (4) occurs readily at the α-position to an olefinic double bond (because the radical R· is then resonance stabilised), and more readily at a tertiary carbon atom than at a secondary carbon atom.[19] In the autoxidation of ethyl chaulmoograte, the mesomeric radical (XIV) would thus be expected to be the principal intermediate, and (XV) relatively unimportant.

Less is known of the way in which a mesomeric radical such as (XIV) will react with molecular oxygen (eqn. 3) to give the secondary (XVI) or the tertiary (V) hydroperoxide. Much of the older work in the literature would obviously warrant reinvestigation, but there are reasonably well-established precedents for the formation of only the secondary hydroperoxide (eqn. 5),[20] or only the tertiary hydroperoxide (eqn. 6),[21] or both (eqn. 7).[22]

Some preliminary evidence that ethyl chaulmoograte in fact gives the tertiary hydroperoxide (V) as, at least, the principal product was obtained by showing that the corresponding saturated alcohol (VII) could not be esterified with phthalic anhydride in the presence of pyridine under the conditions where cyclopentanol gives the hydrogen phthalic ester; this unreactivity is characteristic of a tertiary alcohol. This structure was

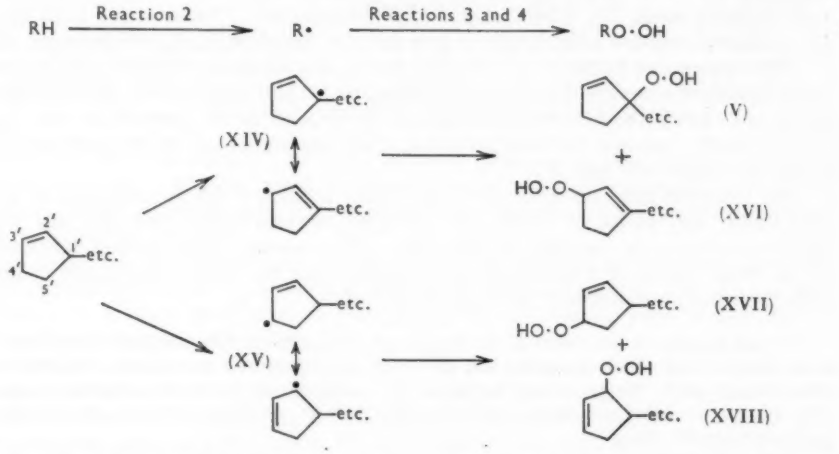
* One "initial ozonide" (of *trans*-di-t-butylethylene) has recently been isolated [18] at −75°. It is not yet known whether it has the structure (IXa) or the oxoxide structure (IXb), but the former appears rather more probable.



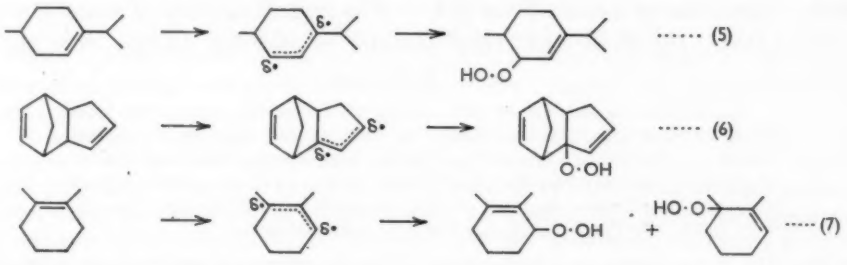
[17] Reviewed by Bailey, *Chem. Rev.*, 1958, **58**, 5.
[18] Criegee and Schröder, *Chem. Ber.*, 1960, **93**, 689.
[19] See, *e.g.*, Bolland, *Quart. Rev.*, 1949, **3**, 1; *Trans. Faraday Soc.*, 1960, **46**, 358; Russell, *J. Amer. Chem. Soc.*, 1956, **78**, 1047.
[20] Hoch and Lang, *Ber.*, 1942, **75**, 300.
[21] Hoch and Depke, *Chem. Ber.*, 1951, **84**, 386.
[22] Farmer and Sundralingham, *J.*, 1942, 121; Farmer and Sutton, *J.*, 1946, 10.

substantiated by a study of the optical asymmetry of the hydroperoxide and its related compounds.

Ethyl chaulmoograte is optically active, $[\alpha]_D$ +51·0° (in chloroform), by virtue of asymmetry centred on the 1′-carbon atom. As the purity of the derived hydroperoxide



increases, its rotatory power decreases. The purest product obtained chromatographically (92% pure) had a specific rotation of +1·6°, and we believe (see below) even this is due to the presence of a non-hydroperoxidic impurity of uncertain structure. This impurity



could be further separated by countercurrent extraction, leaving the hydroperoxide (86% pure, from a different preparation), $[\alpha]_D$ +0·8° (in ethanol).*

Reduction of the impure hydroperoxide to the corresponding unsaturated alcohol with sodium borohydride (which may be assumed to proceed with retention of configuration [23]) gave no significant change in the small optical rotation; † this is the result which would be expected if the hydroperoxide was optically inactive, and the impurity was optically active and chemically inert. Hydrogenation of the impure hydroperoxide caused inversion of the sign of rotation (*e.g.*, 81% pure hydroperoxide, $[\alpha]_D$ +6·8° ⟶ $[\alpha]_D$ −4·0°), showing that the impurity was not the parent ethyl chaulmoograte (III)

* This essentially zero rotation affords additional evidence against the oxoxide structure (IV), which would be expected to be optically active; a homolytic reaction initiated at the asymmetric (1′) centre, on the other hand, might be expected to give an inactive hydroperoxide (V and/or XVI).

† Again this argues against the oxoxide structure (IV) which might be expected to be reduced to the epoxide (VIII) which we know to have a specific rotatory power of +20°.

[23] Davies and Feld, *J.*, 1956, 665; 1958, 4673; Davies, *J.*, 1958, 3474.

(which would give the symmetrical dihydrochaulmoograte), or apparently the epoxide (VIII) (which we found to be unreactive under these conditions).

Impure ethyl hydroxychaulmoograte, obtained by borohydride reduction of the hydroperoxide, was hydrolysed to the impure hydroxy-acid ($[\alpha]_D$ +6·0° and +6·5° in two experiments). Two recrystallisations of the brucine salts from ethyl acetate gave the pure hydroxy-acids, $[\alpha]_D$ +24·1° and +18·0° respectively. These active acids absorbed the calculated amount of hydrogen to give inactive dihydrohydroxychaulmoogric acid.

The unsaturated hydroxy-acid must therefore be optically asymmetric, the asymmetry being destroyed when the double bond is saturated. This can only mean that the hydroxy-group, and hence the hydroxyperoxy-group, is situated at the junction of the ring and the side-chain, and that the double bond is in the unsymmetrical (2',3') position as shown in the structures (VI) and (V).

We conclude that the hydroperoxide which is formed by autoxidation is at least principally, and probably wholly, the tertiary compound (V), and that the reaction involves extensive or complete racemisation. This appears to be the first demonstration of the steric course of a homolytic autoxidation, and the results are clearly compatible with the mechanism outlined in reactions (2)—(4).

We are grateful to Professor E. D. Hughes, F.R.S., and Sir Christopher Ingold, F.R.S., for their interest and encouragement, and to Dr. E. M. Thain and the Director of the Tropical Products Institute for providing facilities for carrying out the counter-current separation. This work was carried out during the tenure (by J. E. P.) of a Commission in the New Zealand Defence Scientific Corps.

William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1. [*Received, May 1st,* 1961.]

---

865. *Solvation of Ions. Part III.*[1] *The S_N2 Reactivity of Some Group VI Anions, Pyridine, and Alkyl Halides in Dipolar Aprotic Solvents.*

By A. J. Parker.

Nucleophilic tendencies of some Group VI anions decrease in the series $SeCN^- > SCN^-$ and $PhS^- > PhO^-$ in both protic and dipolar aprotic solvents. The rate of a typical S_N2 reaction between dipolar molecules is not appreciably influenced by the change from protic to dipolar aprotic solvent. The solvent influence on rates of S_N2 reactions of alkyl halides does not vary as the alkyl group is changed in a homologous series.

In Part II[1] it was shown that nucleophilic tendencies of anions are different in dipolar aprotic and in protic solvents, the former solvents appearing to "level" these tendencies. Towards alkyl halides in acetone there is the series $Br^- > Cl^-$, I^- with small differences, whereas in methanol or water the order is $I^- > Br^- > Cl^-$ and the differences are large. The relative tendencies towards methyl iodide of thiocyanate, azide, and chloride ions were markedly affected by the change from methanol to dimethylformamide.[1] We have now extended this work to some halogen-like anions, whose nucleophilic atom (*i.e.*, the atom forming a new bond with carbon) was a Group VI element, in two types of bimolecular nucleophilic replacement, namely, thiocyanate and selenocyanate ions with methyl iodide, and thiophenoxide and phenoxide ions with *p*-iodonitrobenzene, all in both methanol and dimethylformamide.

The kinetic results, summarized in Table 1, lead to the following conclusions: In both methanol and dimethylformamide, potassium selenocyanate reacts faster than potassium thiocyanate with methyl iodide, and sodium thiophenoxide faster than sodium phenoxide with *p*-iodonitrobenzene. The nucleophilic tendencies of $SeCN^-$ and SCN^-, and of PhS^-

[1] Part II, Parker, *J.*, 1961, 1328.

XUM

TABLE 1.

Reactions of Group VI nucleophiles in protic and in dipolar aprotic solvents. Rate constants (k_2; l. mole^{-1} sec.$^{-1}$) at 0°. Equimolar proportions of reactants initially at 0·03—0·04M.

	10^4k_2 in MeOH	10^4k_2 in H·CO·NMe$_2$	$\frac{k_2(\text{H·CO·NMe}_2)}{k_2(\text{MeOH})}$
MeI + NCS$^-$	0·20 [a]	117	585
MeI + NCSe$^-$	4·0	916	229
p-NO$_2$·C$_6$H$_4$I + PhS$^-$	0·034 [b]	820	$2·4 \times 10^4$
p-NO$_2$·C$_6$H$_4$I + PhO$^-$	0·004 [b]	0·066 [b]	$1·7 \times 10^5$

[a] Ref. 1. [b] Extrapolated from rates at higher temperatures (Table 4).

and PhO$^-$ are levelled slightly by the change from protic to dipolar aprotic solvent, as might be expected.[1] Thiophenoxide ion is much more susceptible than thiocyanate ion to solvent change, suggesting that, in methanol, hydrogen bonding contributes more to the solvation of the former.[1]

Now that it has been established that the nucleophilic tendencies of similarly constituted Group VI nucleophiles are in the same order in both classes of solvent, it is reasonable to attribute part of their nucleophilic tendencies to the nucleophile itself, rather than to differential solvation of the nucleophile.

Nucleophilic tendencies generally increase, within a group of the Periodic Table, with the atomic number of the atom forming the new bond to carbon.[2] This leads to the nucleophilic tendencies SeCN$^-$ > SCN$^-$ > OCN$^-$ and PhSe$^-$ > PhS$^-$ > PhO$^-$. The nucleophilic tendency of RM$^-$, where *M* is a Group VI atom and R is a group satisfying the valency requirements of M, will be reduced by any contribution made by the second resonance structure of the pair R–M$^-$ ⟷ $^-$R=M. Conjugative electron withdrawal by R favours the latter structure, leading to the nucleophilic tendencies PhS$^-$ > NCS$^-$ (ref. 3) and PhO$^-$ > p-NO$_2$·C$_6$H$_4$·O$^-$ > 2,4-(NO$_2$)C$_6$H$_3$·O$^-$ (ref. 4). Conjugative electron release from M to the same R group favours structure $^-$R=M and decreases in the series [3,5] RO$^-$ > RS$^-$ > RSe$^-$, leading to the nucleophilic tendencies NCSe$^-$ > NCS$^-$ > NCO$^-$ and PhSe$^-$ > PhS$^-$ > PhO$^-$. It is relevant that OCN$^-$ forms isocyanates,[6] SCN$^-$ usually forms thiocyanates,[6] and SeCN$^-$ always forms selenocyanates [7] in S_N2 reactions with alkyl halides.

Thus both factors, the ability of M$^-$ to form a bond with carbon and the interaction between R and M$^-$, lead to the same nucleophilic tendencies in a series RM$^-$. Nucleophilic tendencies of Group VII anions do not increase with increasing atomic number in media where hydrogen-bonding solvation forces are absent,[1] and this might suggest that interactions between R and M$^-$ largely account for the nucleophilic tendencies of Group VI anions in dimethylformamide.

Many investigations of S_N2 reactions between dipolar molecules in a variety of solvents have been reported.[8,9] The rates suggest that this class of reaction is not greatly affected by the change from a protic to a dipolar aprotic solvent, provided that the dielectric constant and ionic strength of the medium are standardized. Some anomalies exist, however,[10] so the rates of the reaction between pyridine and butyl bromide in dimethylformamide, in methanol, and in aqueous methanol have been measured under

[2] Hine, "Physical Organic Chemistry," McGraw-Hill, New York, 1956.
[3] Parker, "Sulfur Nucleophiles in S_NAr Reactions," in "Organic Sulfur Compounds," Pergamon, London, 1961.
[4] Leahy, Liveris, Miller, and Parker, *Austral. J. Chem.*, 1956, **9**, 382.
[5] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, New York, 1953.
[6] Sidgwick, "Organic Chemistry of Nitrogen," Oxford Univ. Press, Oxford, 1937.
[7] Houben-Weyl, "Methoden der Organischen Chemie," Vol. IX, G. Thieme, Stuttgart, 1955.
[8] Hinshelwood and his co-workers, *J.*, 1938, 858, 1786, and earlier papers; Popvici and Pop, *Compt. rend.*, 1957, **245**, 846.
[9] Coleman and Fuoss, *J. Amer. Chem. Soc.*, 1955, **77**, 5472; Kronick and Fuoss, *ibid.*, p. 6114; Fuoss and Hirsch, *ibid.*, p. 6115.
[10] Palit, *J. Org. Chem.*, 1947, **12**, 752.

standard conditions. The results can be compared with those obtained by Fuoss and his co-workers [9] who used other solvents (cf. Table 2). It is clear that the rate of reaction

TABLE 2.

Reactions of pyridine with butyl bromide in protic and in dipolar aprotic solvents of similar dielectric constant, at the same ionic strength. Rate constants (k_2; l. mole^{-1} sec.$^{-1}$) at 50°. [Pyridine]$_0$ = 0·2M; [butyl bromide]$_0$ = 0·1M.

Solvent	ε	10^6k_2	Solvent	ε	10^6k_2
Sulpholan [b]	42·0	61 [a]	MeOH	33	18
4 : 1 v/v MeOH–H_2O	42	21	Dimethylsulpholan [c]	29·5	21 [a]
H·CO·NMe_2	37	30	2-Methyl-1,3-dioxolan	65·1	37 [a]

[a] Ref. 9. [b] Tetrahydrothiophen 1,1-dioxide. [c] Tetrahydro-2,4-dimethylthiophen 1,1-dioxide.

TABLE 3.

Effect of different alkyl groups on solvent influence on the rate of Finkelstein substitutions. Rate constants (k_2) are in l. mole^{-1} sec.$^{-1}$. Equimolar proportions of reactants, initially 0·02—0·04M.

	10^4k_2 in MeOH	10^4k_2 in H·CO·NMe_2	$\frac{k_2(\text{H·CO·NMe}_2)}{k_2(\text{MeOH})}$
MeI + LiCl at 0°	0·0011 [a]	1300	1·2 × 10^6
EtI + LiCl at 0°	0·00043	630	1·5 × 10^6
Pr^nI + LiCl at 0°	0·00028	480	1·7 × 10^6
	10^4k_2 in MeOH	10^4k_2 in acetone	$\frac{k_2(\text{acetone})}{k_2(\text{MeOH})}$
MeBr + LiCl at 25°	0·046 [c]	5950 [b]	1·3 × 10^5
Pr^nBr + LiCl at 25°	0·00049	64 [b]	1·3 × 10^5

[a] Ref. 1. Ingold, *Quart. Rev.*, 1957, **11**, 1. [c] Moelwyn-Hughes, *Trans. Faraday Soc.*, 1939, **35**, 368.

of pyridine with butyl bromide is not appreciably influenced by the solvent provided that the dielectric constant and salt effect are standardised. This confirms the view that the dipolar aprotic–protic solvent effect observed for S_N2 reactions [1] applies only when at least one of the reactants is an anion. For this reason, equilibria (*a*) and (*b*) (R's are alkyl) will lie much further to the left in dipolar aprotic than in protic solvents of the same dielectric constant:

$$R_3N + R'X \rightleftharpoons R'R_3N^+ X^- \quad (a)$$

$$R_2S + R'X \rightleftharpoons R'R_2S X^- \quad (b)$$

$$RX + Y^- \longrightarrow RY + X^- \quad (c)$$

To establish whether the effect of solvent on the rate of reaction (*c*) depended on the nature of R, the rates of reaction of methyl, ethyl, and propyl iodide with lithium chloride in methanol and in dimethylformamide, and of propyl bromide with lithium chloride in methanol were measured under standard conditions. Table 3 shows that variation of the alkyl group R does not influence the solvent effect in these cases. S_N2 reactions of propyl halides are as susceptible to the change from protic to dipolar aprotic solvent as the corresponding reactions of the same methyl halides.

EXPERIMENTAL

Materials.—Solvents, substrates, lithium chloride, pyridine, and potassium thiocyanate were purified by methods already described.[1,9,11] Dimethylformamide was purified in the usual way,[11] then passed through a molecular sieve. Its purity was confirmed by gas chromatography. Rates in this grade of solvent were identical with those obtained in earlier work.[1] Potassium selenocyanate of reagent grade, dried *in vacuo*, was made into stock solutions in dimethylformamide and in methanol, which were stable under the conditions used. These stock solutions were tested potentiometrically [1] for other anions which give insoluble silver salts and were standardised against silver nitrate before use. The pH of aqueous solutions was 5—6.

Sodium thiophenoxide and sodium phenoxide were obtained from thiophenol and phenol,

[11] Miller and Parker, *J. Amer. Chem. Soc.*, 1961, **83**, 117.

respectively, by treatment with an equivalent amount of sodium hydroxide solution. They were crystallised from a little water, then twice from acetone–ether, and were dried under a vacuum.

Kinetics.—All reactions followed second-order kinetics for at least 70% reaction. The procedure for study of reactions of alkyl halides with halide ions has been described.[1] The reactions of selenocyanate ions with methyl iodide were followed in the same way. Control measurements showed that iodide and selenocyanate ions could be estimated separately in their mixtures by potentiometric titration with silver nitrate, in the presence of barium nitrate, by use of a silver wire and calomel electrode. Total halogenoid content and pH remained constant throughout. New results are in Table 4.

TABLE 4.

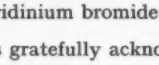
Rate constants (k_2; l. mole^{-1} sec.$^{-1}$) for reactions in methanol and dimethylformamide.

	10^4k_2 in MeOH	10^4k_2 in H·CO·NMe$_2$
MeI + KSCN	—	117 [0°]
MeI + KSeCN	4·0 [0·0°]; 91·3 [25·0°]	916 [0°]
EtI + LiCl	0·035 [35·8°]; 0·47 [59·8°]	63 [0°]
Pr^{n}I + LiCl	0·024 [35·8°]; 0·31 [59·8°]	48 [0°]
Pr^{n}Br + LiCl	9·2 [100·0°]; 84·5 [123·1°]	—
p-NO$_2$·C$_6$H$_4$I + PhONa	0·145 [100·0°]; 1·18 [123·1°]	6·7 [35·8°]; 100 [59·8°]
p-NO$_2$·C$_6$H$_4$I + PhSNa	8·80 [50·0°]; 12·6 [55·0°] 55·5 [69·9°]; 504 [100·0°]	823 [0°]

Reactions of pyridine with butyl bromide were followed by stopping reaction of samples with dilute nitric acid and titrating the bromide ion. Methanol, dimethylformamide, and 4 : 1 v/v methanol–water (of dielectric constant equivalent to that of sulpholan [9]) were used as solvents. New results are in Table 2.

Reactions of sodium thiophenoxide and sodium phenoxide with *p*-iodonitrobenzene in methanol were carried out in the presence of a ten-fold excess of thiophenol and phenol, respectively, to prevent methanolysis and subsequent attack by methoxide ion.[4] The dry sodium salts were used without their conjugate acids in dimethylformamide, because phenol and thiophenol are strong hydrogen-donors and would reduce the rate of reaction. Reactions were carried out under nitrogen, in solutions flushed out with nitrogen, as a precaution against oxidation of thiophenoxide or iodide. Reaction of samples of thiophenoxide reactions were stopped in hydrochloric acid and unconsumed hydrochloric acid was estimated (pH meter to detect the end point). Iodide ion could not be estimated in the presence of thiophenol. Reactions of phenoxide ion were followed by estimating both unconsumed phenoxide and iodide ion; the total remained constant throughout reaction. Rates are in Table 4.

Reaction Products.—The alkyl halide–halogen (etc.) exchanges were replacements, since total halogen was constant and no acid was formed. Each anion was identified by the characteristic potential at the end point of a silver ion titration. No cyanide ion was detected during the reaction of methyl iodide with potassium selenocyanate, and the characteristically evil-smelling methyl selenocyanate,[7] b. p. 155°, was isolated in 80% yield from reaction in both solvents. The crude product, freed from selenocyanate ion, gave hydrogen cyanide with concentrated hydrochloric acid, confirming the expectation that selenocyanate and not isoselenocyanate was the major product.[7]

p-Iodonitrobenzene gave *p*-nitrophenyl phenyl sulphide, m. p. 55°, with sodium thiophenoxide, and *p*-nitrophenyl phenyl ether, m. p. 60°, with sodium phenoxide, in both methanol and dimethylformamide. Mixtures of sodium thiophenoxide with *p*-iodonitrobenzene in dimethylformamide became momentarily blue, then deep green, and finally red at the completion of reaction. The green colour may be that of the complex  in dimethylformamide.[11]

Butyl bromide was not hydrolysed by 4 : 1 methanol–water or methanol under the conditions of its reaction with pyridine. 1-Butylpyridinium bromide is the product of this reaction.[9]

The support of an I.C.I. Fellowship is gratefully acknowledged. I thank Professor E. D. Hughes for reading the manuscript.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER STREET,
LONDON, W.C.1.

[*Received, June 5th,* 1961.]

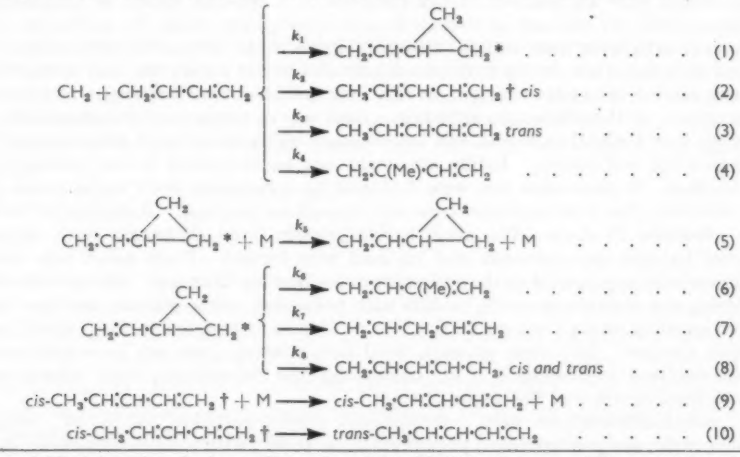
866. *The Reaction of Methylene with Buta-1,3-diene.*

By Barbara Grzybowska, J. H. Knox, and A. F. Trotman-Dickenson.

Methylene (from the photolysis of keten and diazomethane) reacts with buta-1,3-diene by (i) insertion into the C–H bonds and (ii) addition to form vinylcyclopropane. At low pressures the vinylcyclopropane isomerizes by fission of the C–C bond β to the double bond. The isomerization, unlike that of the alkylcyclopropanes, goes little beyond 50% completion. It is suggested that this behaviour is associated with the formation of electronically excited vinylcyclopropane.

The combination of methylene with a hydrocarbon to yield a cyclopropane or cyclobutane derivative is so exothermic that the resultant molecule is chemically activated and will either isomerize or decompose unless it loses its excess of energy. The products are similar to those formed when cyclanes, activated by thermal collisions, react. This pattern of behaviour has been observed for cyclopropane [1] from ethylene,[2] methylcyclopropane [3] from propene [4,5] and cyclopropane,[4,6] 1,1-dimethylcyclopropane [7] from isobutene,[8] 1,2-dimethylcyclopropane [9] from but-2-ene,[10] and methylcyclobutane [11] from cyclobutane.[12] The object of the present work was to study the reactions of vinylcyclopropane activated by the exothermicity of the addition of methylene to buta-1,3-diene. The thermal isomerization of vinylcyclopropane probably cannot be investigated because at the necessary high temperatures side reactions are bound to interfere. This is the first example of the study of a reaction by synthetic activation that could not be conventionally investigated.

The following reaction scheme was expected by analogy with similar systems:


CH2 + CH2:CH·CH:CH2
k1 → CH2:CH·CH(CH2)—CH2 * (1)
k2 → CH3·CH:CH·CH:CH2 † cis (2)
k3 → CH3·CH:CH·CH:CH2 trans (3)
k4 → CH2:C(Me)·CH:CH2 (4)
CH2:CH·CH(CH2)—CH2 * + M —k5→ CH2:CH·CH(CH2)—CH2 + M (5)
CH2:CH·CH(CH2)—CH2 *
k6 → CH2:CH·C(Me):CH2 (6)
k7 → CH2:CH·CH2·CH:CH2 (7)
k8 → CH2:CH·CH:CH·CH3, cis and trans (8)
cis-CH3·CH:CH·CH:CH2 † + M → cis-CH3·CH:CH·CH:CH2 + M (9)
cis-CH3·CH:CH·CH:CH2 † → trans-CH3·CH:CH·CH:CH2 (10)

[1] Chambers and Kistiakowsky, *J. Amer. Chem. Soc.*, 1934, **56**, 399; Corner and Pease, *ibid.*, 1945, **67**, 2067; Pritchard, Sowden, and Trotman-Dickenson, *Proc. Roy. Soc.*, 1953, *A*, **217**, 563; Rabinovitch, Schlag, and Wiberg, *J. Chem. Phys.*, 1958, **28**, 504; Falconer, Hunter, and Trotman-Dickenson, *J.*, 1961, 609.

[2] Frey, *J. Amer. Chem. Soc.*, 1957, **79**, 1259; Frey and Kistiakowsky, *ibid.*, p. 6373.

[3] Chesick, *J. Amer. Chem. Soc.*, 1960, **82**, 3277.

[4] Knox and Trotman-Dickenson, *Chem. and Ind.*, 1957, 1039.

[5] Butler and Kistiakowsky, *J. Amer. Chem. Soc.*, 1960, **82**, 759.

[6] Butler and Kistiakowsky, *J. Amer. Chem. Soc.*, 1961, **83**, 1324.

[7] Flowers and Frey, *J.*, 1959, 3953.

[8] Wells, Knox, and Trotman-Dickenson, *J.*, 1958, 2897; Frey, *Proc. Roy. Soc.*, 1959, *A*, **250**, 709.

[9] Frey, *Proc. Roy. Soc.*, 1960, *A*, **257**, 122; 1961, *A*, **260**, 424.

[10] Frey, *Proc. Roy. Soc.*, 1959, *A*, **251**, 579.

[11] Das and Walters, *Z. phys. Chem.* (*Frankfurt*), 1958, **15**, 22.

[12] Frey, *Trans. Faraday Soc.*, 1960, **56**, 1201.

The asterisk and dagger indicate that there is evidence that the designated molecules are activated.

In accordance with this scheme, it is found that when keten is photolysed in a Pyrex reaction vessel above 500 mm. pressure, the products are: vinylcyclopropane, 90·0%; penta-1,4-diene, 1·6%; isoprene, 2·4%; *cis*-penta-1,3-diene, 2·4%; and *trans*-penta-1,3-diene, 3·6%. These figures were obtained on the assumption that equal amounts of each hydrocarbon yielded equal peak areas on the recorder fed from the thermal conductivity gauge of the chromatographic system, which is probably correct within 1—2%. Since penta-1,4-diene can arise only by isomerization of vinylcyclopropane its amount should be added to that of the cyclic compound in order to calculate the relative reactivity of C–H and C=C double bonds. Hence we find that (Reactivity C=C)/(Reactivity C–H) = 33. There is little difference in the reactivities of the central and terminal C–H bonds. The relative reactivities of the double and the single bond in C=C–H depend considerably upon the source and wavelength of actinic light used to produce the methylene. Results of different workers on different systems cannot be readily compared, but it appears that the conjugation slightly activates the double C=C bond relative to the vinyl C–H bond.

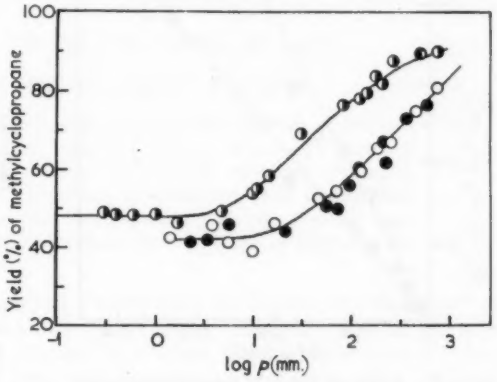


FIG. 1. Variation, with pressure, of yield of vinylcyclopropane on addition of methylene to buta-1,3-diene.

◑ Methylene from keten, Pyrex vessel.
○ Methylene from diazomethane, Pyrex vessel.
● Methylene from diazomethane, quartz vessel.

Below 500 mm. pressure the yield of vinylcyclopropane declines as shown in Fig. 1. At first the decline is similar to that found in the addition of methylene to other olefins and a plot of the reciprocal of the pressure against

$$\frac{\text{Proportion of vinylcyclopropane isomerised}}{\text{Proportion of vinylcyclopropane deactivated by collison}} = \frac{k_6 + k_7 + k_8}{k_5[\mathrm{M}]}$$

yields the predicted straight line (Fig. 2) when the methylene is derived from the photolysis of keten and of diazomethane.

Hence $(k_6 + k_7 + k_8)/k_5 = 0{\cdot}03$ (keten) and 0·058 (diazomethane) atm.$^{-1}$. As can be seen from the Table these results are in good agreement with what might be expected for a

The relative rates of reaction of cyclanes.

Compound	Thermal isomn., 10^4k (sec.$^{-1}$), at 475°	k(isomn.)/k(deactivn.) * (atm.$^{-1}$): $^1CH_2$ from $CH_2{:}CO$	$^1CH_2$ from CH_2N_2	Ref.
Cyclopropane	1·1	1·19	—	1, 2
Methylcyclopropane	2·8			3
from cyclopropane		0·284	0·44	5
from propene		0·06	0·120	6
1,1-Dimethylcyclopropane	5·7	0·003	0·02	7, 8
1,2-Dimethylcyclopropane	2·9	—	0·02	9, 10
Vinylcyclopropane	—	0·03	0·06	This work
Methylcyclobutane	31	0·05	0·25	11, 12

* The values of k(isomerization)/k(deactivation) are sometimes not known to better than ±30%.

cyclopropane derivative containing five carbon atoms which is rather more reactive than the alkyl-substituted compounds.

The yield of isoprene remains constant throughout our pressure range (Fig. 3). Presumably it is only formed in the initial addition of methylene to the olefin, and reaction 6 is negligible. Evidently vinylcyclopropane isomerizes only by mechanisms that involve the rupture of the C–C bond β to the double bond. This preferred rupture can readily be understood if the primary step is formation of a biradical by direct rupture. This would lead to a stable allylic radical on rupture of the β bond but not on rupture of the γ-bond. The observation provides some support for the mechanism of cyclopropane isomerization favoured by Rabinovitch and his co-workers.[1]

The most striking observation is the limit below which the proportion of vinylcyclopropane in the products never falls. No other system has been found to exhibit this behaviour. That the limit is real is clearly shown in Fig. 1. It appears that there is a slight difference in the limits for methylene derived from keten and from diazomethane.

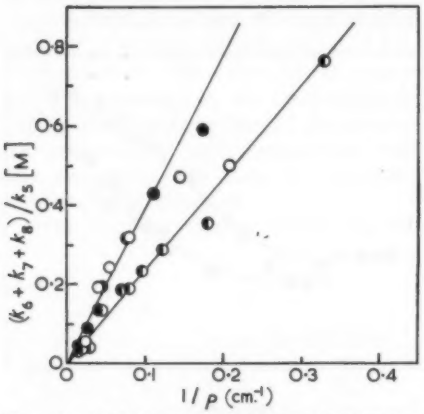


FIG. 2. Relative rates of isomerization and deactivation of activated vinylcyclopropane as a function of pressure. For open, full, and half-full circles see FIG. 1.

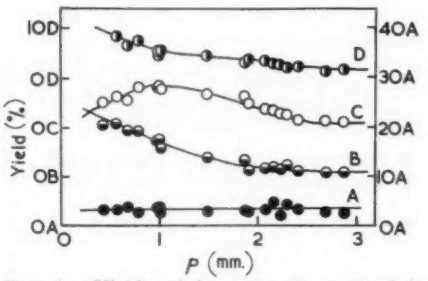


FIG. 3. Yields of isoprene ●, penta-1,4-diene ◒, *cis*-penta-1,3-diene ○, and *trans*-penta-1,3-diene ◑ from the photolysis of keten with buta-1,3-diene in a Pyrex vessel at room temperature.

The phenomenon is probably connected with the presence of the vinyl group; no other unsaturated cyclopropane derivative has been investigated. The exothermicity of the methylene addition is so great that an electronically excited state of a compound containing π-electrons could be formed. The electronically excited molecule might then either lose energy by fluorescence, or be deactivated by collision, provided that its lifetime, with respect to isomerization, is long. Approximately half the adducts do not isomerize; possibly these molecules are formed in an electronically excited state either from the singlet or from the triplet methylenes released on photolysis.

The results shown in Fig. 3 also show that the *cis*-penta-1,3-diene is initially activated. At low pressures it isomerizes to the *trans*-compound before it is deactivated, despite the lower free energy of formation of the *cis*-compound at room temperature. It is possible that for such activated molecules the free energy of formation at very high temperatures is the relevant quantity. Above 1300° K the *trans*-compound is the more stable.

Experimental.—Pyrex and quartz reaction vessels of between 20 and 5000 c.c. were attached to a conventional high-vacuum system. They were kept slightly below room temperature by water streaming over them. The light source was an unfiltered 125 w medium-pressure mercury arc.

Butadiene sulphone (dihydrothiophen dioxide) was thermally decomposed to butadiene and sulphur dioxide which was absorbed by 20% aqueous potassium hydroxide and in several bulb-to-bulb distillations over solid potassium hydroxide. Methylene was generated from keten and from diazomethane. Keten was prepared by the pyrolysis of acetic anhydride and purified by bulb-to-bulb distillation. Diazomethane was made by reaction of potassium hydroxide in ethylene glycol on *N*-methylnitrosourethane and was swept by a stream of nitrogen through a potash tube and a coil cooled in ice-salt into a trap cooled in liquid nitrogen: No impurities could be detected by gas chromatography.

The products were analysed by gas chromatography with hydrogen as the carrier gas at the optimum flow rate of 45 c.c. min.$^{-1}$ and a 20 ft. coil of copper tubing, cooled in ice, packed with 5% squalane–Celite (80—100 mesh). The detector was a thermal conductivity cell with tungsten filaments. Products were identified by comparison of their retention times, on different column packings, with known samples (when these were available) and by infrared spectroscopy.

CHEMISTRY DEPARTMENT, EDINBURGH UNIVERSITY.
EDWARD DAVIES CHEMICAL LABORATORY, ABERYSTWYTH. [*Received, June 5th*, 1961.]

---

867. *Mesityl and Phenyl Derivatives of Lead.*

By F. GLOCKLING, K. HOOTON, and D. KINGSTON.

Lead chloride or bromide reacts rapidly with phenyl-lithium or phenyl- or mesityl-magnesium bromide in tetrahydrofuran at −40°. Deeply coloured solutions result which involve equilibrium mixtures, $PbAr_2 + ArLi(MgX) \rightleftharpoons Ar_3Pb{\cdot}Li(MgX)$. Evidence is presented that diaryl-leads are rapidly hydrolysed even at low temperatures, giving a basic lead bromide. Bromination studies indicate that dimesityl-lead is produced by carbonation of $(Mesityl)_3Pb{\cdot}MgBr$.

THE isolation of diphenyl- and di-*p*-tolyl-lead was reported by Krause and Reissaus [1] in 1922. They treated anhydrous lead chloride with ethereal phenylmagnesium bromide at +2° and obtained a deep red-brown solution from which, after hydrolysis at 0°, they isolated diphenyl-lead by extraction into benzene and precipitation with ethanol. Diphenyl-lead obtained in this way (4—5% yield) is described as a blood-red, air-sensitive, amorphous powder which is decolorised when heated above 100° and is monomeric in benzene solution. More recently Gilman and his co-workers [2] investigated the apparently analogous reaction between lead chloride and phenyl-lithium in ether. They obtained evidence for the equilibrium, $Ph_3Pb{\cdot}Li \rightleftharpoons PbPh_2 + PhLi$, based on the appearance of a positive Gilman colour test when more than 2·8 moles of phenyl-lithium were used per mole of lead chloride. Hydrolysis of such solutions (which might have been expected to produce diphenyl-lead) gave a heavy yellow precipitate and a red or yellow ether solution. Attempts to isolate diphenyl-lead were unsuccessful. In contrast to the deep red solutions (presumably of diphenyl-lead) obtained by Krause and Reissaus, Gilman *et al.* found that using two moles of phenyl-lithium and one of lead chloride in ether at −10° led to a yellow solution that gave a negative colour test, deposited lead when boiled, and on hydrolysis afforded hexaphenyldilead in 79% yield:

$$PbCl_2 + 2PhLi \xrightarrow[-10°]{Et_2O} PbPh_2 \xrightarrow{Reflux} Pb + Pb_2Ph_6$$

Solutions of triphenyl-leadlithium in boiling ether were, by contrast, stable.

We have made further studies on the reaction of lead halides with both Grignard and aryl-lithium reagents with a view to obtaining diphenyl- and dimesityl-lead. Our attempts

[1] Krause and Reissaus, *Ber.*, 1922, **55**, 888.
[2] Gilman, Summers, and Leeper, *J. Org. Chem.*, 1952, **17**, 630.

to repeat the work of Krause and Reissaus have been unsuccessful: we find that hydrolysis, at 0°, of the deeply coloured ether solutions containing diphenyl-lead results in discharge of the colour.

Reactions of Lead Chloride and Bromide with Phenyl-lithium.—The reaction of lead chloride with phenyl-lithium in ether is reported [2] as being slow below −10°. In contrast, with tetrahydrofuran as solvent, the reaction is rapid even at −40°, giving yellow-green solutions, and does not involve separation of lead. When either 2 or 3 moles of phenyl-lithium were used per mole of lead bromide hydrolysis then gave a copious dense yellow precipitate (cf. ref. 2) which we have characterised as lead oxide bromide [$3PbO,PbBr_2$ ($1—3H_2O$)] contaminated with 1—2% of hexaphenyldilead. No diphenyl-lead is isolable in either case, even after hydrolysis at −30°. This behaviour is compatible with the equilibrium suggested by Gilman *et al.*, but also implies that diphenyl-lead is itself highly susceptible to hydrolysis (Krause and Reissaus claimed that they isolated diphenyl-lead *after* hydrolysis of reaction mixtures):

$$Ph_3Pb{\cdot}Li \rightleftharpoons PbPh_2 + PhLi \xrightarrow{H_2O} LiOH + C_6H_6 + Pb(OH)_2$$

If lead hydroxide is suspended in a tetrahydrofuran solution of magnesium bromide and the mixture subsequently hydrolysed, a basic lead bromide is isolated.

The isolation of small quantities of hexaphenyldilead without simultaneous production of metallic lead could be accounted for by the hydrolysis of undissociated triphenyl-lead-lithium followed by thermal decomposition or oxidation of the hydride:

$$Ph_3Pb{\cdot}Li \xrightarrow{H_2O} Pb_2PbH \begin{cases} \longrightarrow Pb_2Ph_6 + H_2 \\ \xrightarrow{O_2} Pb_2Ph_6 + H_2O \end{cases}$$

Hydrolysis of triphenyl-leadlithium in a vacuum apparatus failed to produce hydrogen, and hexaphenyldilead was isolated in 1·4% yield without exposure to air. Much higher yields (~20%) of hexaphenyldilead result if air is not excluded.

When equimolar ratios of phenyl-lithium (or phenylmagnesium bromide) and lead bromide are used in tetrahydrofuran, about half of the lead bromide remains undissolved after the Gilman colour test becomes negative, and treatment of the filtrate with benzyl chloride leads to benzyltriphenyl-lead in 28% yield based on "soluble" lead. Thus we consider that the initial reaction, $PbBr_2 + PhLi \longrightarrow PhPbBr + LiBr$, is slow and that phenyl-lead bromide (which may be soluble in tetrahydrofuran) reacts rapidly to give diphenyl-lead. Moreover, the isolation of benzyltriphenyl-lead under these conditions points to there being triphenyl-leadlithium in equilibrium with diphenyl-lead even when equimolar ratios of phenyl-lithium to lead bromide are initially involved.

Reactions of Lead Bromide with Phenylmagnesium Bromide.—In contrast to reactions involving phenyl-lithium, lead bromide and phenylmagnesium bromide show more distinct colour changes in tetrahydrofuran:

$$PbBr_2 \xrightarrow[1\text{ mol.}]{PhMgBr} \text{Yellow solution} \xrightarrow[1\text{ mol.}]{PhMgBr} \text{Red solution} \xrightarrow[1—3\text{ mol.}]{PhMgBr} \text{Red-brown solution}$$

If the red-brown solutions resulting from an excess of phenylmagnesium bromide are hydrolysed or treated with anhydrous ethanol, the red colour returns momentarily and is followed by the precipitation of a basic lead bromide. Only traces of hexaphenyldilead are produced on hydrolysis, and over 90% of the lead appears as the basic bromide. Removal of tetrahydrofuran from the red solution (2 mol. of PhMgBr) and extraction with methylene chloride gave an orange-red solid which decomposed (giving lead) at room temperature and was sensitive to both air and water. This material contained lead, magnesium, and bromine, and is probably a mixture of $PbPh_2$, $Ph_3Pb{\cdot}MgBr$, and $MgBr_2$–tetrahydrofuran.

Reactions of Lead Bromide with Mesitylmagnesium Bromide.—Some of the difficulties

XUM

encountered in our attempts to isolate diphenyl-lead result from thermal instability, and the reaction of mesitylmagnesium bromide, which showed analogous colour changes and behaviour on hydrolysis, led to considerably more stable products. For example, lead bromide may be heated under reflux in tetrahydrofuran for 4 hr. with a large excess of mesitylmagnesium bromide without separation of metallic lead; more prolonged heating results in the formation of lead and tetramesityl-lead. As in reactions involving phenylmagnesium bromide, these observations are compatible with an equilibrium between dimesityl-lead and trimesityl-leadmagnesium bromide. Failure to isolate more than traces of organolead compounds on treatment with water again points to rapid hydrolysis of mesityl groups.

We have attempted to displace the equilibrium in favour of dimesityl-lead by reaction of trimesityl-leadmagnesium bromide with reagents milder than water. Dry ethanol causes immediate discharge of the colour, but addition of pure carbon dioxide results in intensification of the red colour. Attempts to isolate pure dimesityl-lead from these deep red solutions have not been successful owing to the similar solubility properties of magnesium bromide–tetrahydrofuran complexes. That carbon dioxide does displace the equilibrium, giving dimesityl-lead, $(Mesityl)_3Pb{\cdot}MgBr \rightleftharpoons Pb(Mesityl)_2 + MesitylMgBr \xrightarrow{CO_2} C_6H_2Me_3{\cdot}CO_2MgBr + Pb(Mesityl)_2$, is inferred from comparative bromination experiments. Reaction mixtures corresponding in composition to $(Mesityl)_3Pb{\cdot}MgBr$ on bromination at a low temperature gave trimesityl-lead bromide, whilst under identical conditions dimesityl-lead dibromide is produced by bromination of the deep red material obtained after reaction with carbon dioxide.

Experimental

Lead analyses were carried out by Saunders and Stacey's method.[3] M. p.s are corrected. All reactions were carried out in an atmosphere of dry oxygen-free nitrogen.

Lead Chloride and Phenyl-lithium.—(*a*) Lead chloride (12·5 g., 0·045 mole) was added in several portions during 30 min. to a stirred, deep red solution of phenyl-lithium (0·092 mole) in tetrahydrofuran (150 c.c.) at −60°. At −40° the solution changed rapidly to a yellowish-green, and the Gilman colour test (Michler's ketone) became negative. A sample of this solution deposited lead at room temperature. After being stirred overnight at −78° the mixture was hydrolysed at −30° by aqueous tetrahydrofuran, and extracted with benzene. Filtration gave a yellow solid (12 g.) shown by *X*-ray examination to be a mixture of basic lead chloride and bromide. The yellow benzene extract gave a yellow solid (2 g.) from which hexaphenyldilead (0·4 g., 3%), m. p. 155° (decomp.), was isolated by crystallisation from benzene–ethanol (Found: C, 49·6; H, 3·7. Calc. for $C_{36}H_{30}Pb_2$: C, 49·3; H, 3·5%).

(*b*) Lead chloride (25·75 g., 0·0925 mole) was added to phenyl-lithium (0·09 mole) in tetrahydrofuran (150 c.c.) as described under (*a*). Filtration at −60° gave unchanged lead chloride (13 g., 0·0466 mole). Benzyl chloride (4·2 g., 0·033 mole) was added to the filtrate in 10 min., then the solution was allowed to reach room temperature, and finally it was heated under reflux for 1·5 hr. The resulting mixture, which contained metallic lead, was hydrolysed and filtered in air. Extraction of the solid residue with hot ethanol gave benzyltriphenyl-lead (3·9 g.), m. p. and mixed m. p. 92·5°. Extraction with hot benzene gave tetraphenyl-lead (3·2 g.), m. p. and mixed m. p. 223°. Lead oxide chloride and bromide were also formed. Addition of benzyl chloride to the solution resulting from 2 mol. of phenyl-lithium and 1 mol. of lead chloride at < −25° gave no benzyltriphenyl-lead, and unchanged benzyl chloride was isolated.

Lead Bromide and Phenyl-lithium in Ether.—Lead bromide (12·2 g., 0·033 mole) was added to phenyl-lithium (0·1 mole) in ether (100 c.c.), and the mixture stirred vigorously at −20° for 2 hr. The pale yellow filtrate was connected to a vacuum apparatus, degassed, and hydrolysed by condensing a water–tetrahydrofuran mixture on the solution which was then allowed to attain room temperature. No hydrogen was produced. The ether solution from the hydrolysis was washed with water and filtered under nitrogen. The residue yielded hexaphenyldilead

[3] Saunders and Stacey, *J.*, 1949, 919.

(0·2 g.) and biphenyl (0·1 g.), oxygen being rigorously excluded at all stages. The solid that was precipitated on hydrolysis was free from organic material; its *X*-ray powder photograph corresponded to a lead oxide bromide, $3PbO,\ oBr_2(1—3H_2O)$.

A comparable experiment in which the isolation procedure after hydrolysis was carried out in air led to the isolation of hexaphenyldilead in 20% yield.

Lead Bromide and Phenylmagnesium Bromide.—(*a*) Phenylmagnesium bromide (0·15 mole) in tetrahydrofuran (120 c.c.) was added to a stirred suspension of lead bromide (18·55 g., 0·05 mole) in tetrahydrofuran (50 c.c.) at −20°. Addition of 2 equiv. of phenylmagnesium bromide gave a deep red solution which became yellowish-brown on addition of the third equivalent of Grignard reagent. The mixture was heated to −10° and hydrolysed by dropwise addition of water, which resulted in the momentary return of the deep red colour, followed by precipitation of lead hydroxide bromide (14 g., 92%). In a similar experiment with equimolar ratios of phenylmagnesium bromide and lead bromide a sample of the resulting orange-red solution decomposed, giving lead at room temperature. Hydrolysis again gave lead hydroxide bromide and a trace (~0·1 g.) of hexaphenyldilead.

(*b*) Phenylmagnesium bromide (0·162 mole) in tetrahydrofuran (150 c.c.) was added to lead bromide (0·0545 mole) in tetrahydrofuran (100 c.c.) at −20°, and benzyl chloride (0·053 mole) was added slowly. The mixture was allowed to warm to room temperature and refluxed overnight. Metallic lead (3·6 g., 32%) was separated and the filtrate treated with benzene and water. Extraction of the white precipitate with chloroform gave tetraphenyl-lead (6 g.), the residue being lead hydroxide bromide (0·9 g.). The benzene solution was evaporated and extraction of the residue with ethanol gave benzyltriphenyl-lead (2·5 g.) and tetraphenyl-lead (1·0 g.).

A similar experiment with equimolar ratios of phenylmagnesium bromide and lead bromide (36·7 g.) with benzyl chloride (5·06 g.) gave unchanged lead bromide (16·7 g.), tetraphenyl-lead (8·5 g.), benzyltriphenyl-lead (1·5 g.), lead (2·5 g.), and lead hydroxide bromide (5·3 g.).

(*c*) Phenylmagnesium bromide (0·1 mole) and lead bromide (18·35 g., 0·05 mole) were stirred in tetrahydrofuran (150 c.c.) at −25° for 3 hr. The solvent was removed *in vacuo* at −20°, and dry methylene chloride (100 c.c.) added at −20° to the orange residue. This procedure precipitated some of the magnesium bromide, though the filtrate after removal of methylene chloride at 0° gave an orange-red solid containing lead, magnesium, bromine, and tetrahydrofuran. Addition of benzene produced two layers, one yellow and the other a deep red, each containing both lead and magnesium. The deep red solution on removal of solvent at 0° left a deep red sticky solid which with water gave lead hydroxide bromide and decomposed to a yellow powder in air. No diphenyl-lead was obtained.

Lead Bromide and Mesitylmagnesium Bromide.—(*a*) Mesitylmagnesium bromide (0·093 mole) in tetrahydrofuran (100 c.c.) was added dropwise to a stirred suspension of lead bromide (17·1 g., 0·0465 mole) in tetrahydrofuran at −25° to −30°. Each drop of Grignard solution produced a localised deep red colour which rapidly dispersed, giving a uniform pale yellow colour which deepened as the addition proceeded. The final deep red solution was filtered at −20° from unchanged lead bromide (0·9 g.), and the filtrate was hydrolysed with water which discharged the colour and resulted in the precipitation of lead hydroxide bromide, $PbO,PbBr_2,H_2O$ (11 g., 78%).

(*b*) Mesitylmagnesium bromide (0·1 mole) in tetrahydrofuran (100 c.c.) was added to a stirred suspension of lead bromide (0·033 mole) in tetrahydrofuran (100 c.c.) at −30°. The Gilman colour test became positive after addition of 2·8 equiv. of Grignard reagent. When the solution was a deep blood-red the third equivalent of Grignard reagent gave a deep red-brown solution. This was poured on a large excess of pure dry solid carbon dioxide and left for 1 hr. at −30°. Filtration in nitrogen at −40° gave a deep red solution. A sample of this solution was immediately decolorised on addition of 2 drops of dry ethanol. The main solution was evaporated at −20°, giving a deep red glass which was divided into two parts. One part was allowed to decompose in air at room temperature, then the grey product was extracted with carbon tetrachloride, giving *tetramesityl-lead* as a yellow solid, m. p. 242° (decomp.) (Found: C, 62·1; H, 6·2; Pb, 30·3. $C_{36}H_{44}Pb$ requires C, 63·2; H, 6·5; Pb, 30·3%). Tetramesityl-lead is also produced if lead bromide is heated with a large excess of mesitylmagnesium bromide for 2 days. The colourless residue from the carbon tetrachloride extraction was a mixture of magnesium bromide and lead hydroxide bromide. The second part of the glass was dissolved in methylene chloride (150 c.c.), and the deep red solution treated with hexane (50 c.c.) which

XUM

precipitated some magnesium bromide–tetrahydrofuran complex. Removal of the solvents from the filtrate again gave a red glass (Found: Pb, 11·3; Br, 25·1%).

Dimesityl-lead Dibromide and Trimesityl-lead Bromide.—The reaction between mesitylmagnesium bromide (0·1 mole) and lead bromide (12·2 g., 0·033 mole) was carried out as described above. The filtrate, after carbonation, was concentrated to 100 c.c., then cooled to −50°, and bromine (1·0 g., 5·6 mmoles) in methylene chloride (15 c.c.) was added dropwise. The resulting yellow solution was shaken with sodium hydrogen carbonate solution, washed, and dried. Removal of solvent gave crude *dimesityl-lead dibromide* (1·7 g.), which from carbon tetrachloride–propan-2-ol produced pale yellow crystals, m. p. 198—199° (Found: C, 39·5; H, 3·5; Br, 25·2. $C_{18}H_{22}Br_2Pb$ requires C, 35·7; H, 3·7; Br, 26·4%).

Bromination of trimesityl-leadmagnesium bromide under identical conditions gave *trimesityl-lead bromide*, as colourless needles, m. p. 145—146° [from light petroleum (b. p. 60—80°)] (Found: Br, 11·6. $C_{27}H_{33}BrPb$ requires Br, 12·4%), together with hexamesityldilead.[4]

THE UNIVERSITY, DURHAM. [*Received, June 7th,* 1961.]

[4] Gilman and Bailie, *J. Amer. Chem. Soc.*, 1939, **61**, 731.

---

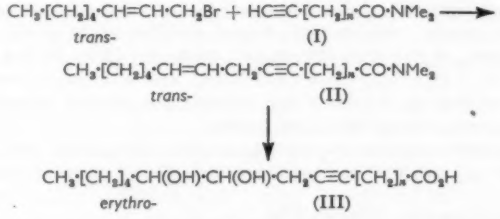
868. *Syntheses of Long-chain Acids. Part II.*[1] *A Synthesis of Linoleic Acid.*

By D. E. AMES and P. J. ISLIP.

Condensation of *NN*-dimethyldec-9-ynamide with *trans*-oct-2-enyl bromide in the presence of sodamide and liquid ammonia gave *trans*-*NN*-dimethyloctadec-12-en-9-ynamide. Treatment of this olefin with perbenzoic acid, followed by hydrolysis, yielded *erythro*-12,13-dihydroxyoctadec-9-ynoic acid which was semihydrogenated and brominated. The resulting oil, containing two isomers of *threo*-9,10-dibromo-*erythro*-12,13-dihydroxyoctadecanoic acid, was converted into the known *threo-threo*-9,10,12,13-tetrabromoctadecanoic acid and thence into linoleic acid.

IN Part I[1] we described the preparation of acetylenic acids by condensation of an alkyl halide with a sodioalkylacetylene, the *NN*-dimethylamide being used as protected carboxyl group in either reactant during the condensation. This procedure has now been extended to the synthesis of long-chain enynoic dimethylamides by the use of an unsaturated alkyl halide.

The readily accessible *NN*-dimethylundec-10-ynamide (I; $n = 8$) was first condensed with *trans*-oct-2-enyl bromide in the presence of sodamide and liquid ammonia, *trans*-*NN*-dimethylnonadec-13-en-10-ynamide (II; $n = 8$) being obtained in 20% yield. Hydroxylation, by treatment with perbenzoic acid and then formic acid, followed by alkaline hydrolysis gave *erythro*-13,14-dihydroxynonadec-10-ynoic acid (III; $n = 8$).



To apply this procedure to the synthesis of linoleic acid, *NN*-dimethyldec-9-ynamide (I; $n = 7$) was prepared from 8-bromo-*NN*-dimethyloctanamide and sodioacetylene.

[1] Ames and Islip, *J.*, 1961, 351, is regarded as Part I.

The sodio-derivative of the acetylenic amide with *trans*-oct-2-enyl bromide gave *trans*-*NN*-dimethyloctadec-12-en-9-ynamide (II; $n = 7$) in 50% yield. Attempts to hydrolyse this to the corresponding acid were unsuccessful owing to the formation of mixtures containing mainly conjugated acids. However, when the olefinic bond in amide (II; $n = 7$) was "protected" by hydroxylation, with perbenzoic acid followed by formic acid, the amide group could be hydrolysed with alkali to afford *erythro*-12,13-dihydroxyoctadec-9-ynoic acid (III; $n = 7$). Complete hydrogenation of the latter gave *erythro*-12,13-dihydroxyoctadecanoic acid.[2]

The acetylenic acid (III; $n = 7$) was semihydrogenated by the method of Cram and Allinger [3] to *erythro-cis*-12,13-dihydroxyoctadec-9-enoic acid (IV). Addition of bromine gave an oil, presumably containing the two possible isomers of *threo*-9,10-dibromo-*erythro*-12,13-dihydroxyoctadecanoic acid (V). This oil was converted into 9,10,12,13-tetrabromoctadecanoic acids (VI) by reaction with hydrogen bromide in acetic–sulphuric acids. Only the isomer, m. p. 114°, which is obtained by addition of bromine to linoleic acid, could be isolated. The expected isomeric acid was presumably present in the oily fraction but could not be obtained crystalline.

Debromination of the ethyl ester of the crystalline tetrabromo-acid gave ethyl linoleate and thence, by alkaline hydrolysis, linoleic acid. The product contained less than 1% of conjugated dienes (as shown by the low intensity of ultraviolet absorption at *ca.* 238

$$\underset{\textit{erythro-}}{CH_3\cdot[CH_2]_4\cdot CH(OH)\cdot CH(OH)\cdot CH_2\cdot CH{=}CH\cdot}\underset{\textit{cis-}}{([CH_2]_7\cdot CO_2H} \quad \text{(IV)}$$

$$\underset{\textit{erythro-}}{CH_3\cdot[CH_2]_4\cdot CH(OH)\cdot CH(OH)\cdot CH_2\cdot CHBr\cdot}\underset{\textit{threo-}}{CHBr\cdot[CH_2]_7\cdot CO_2H} \quad \text{(V)}$$

$$\underset{\textit{threo-}}{CH_3\cdot[CH_2]_4\cdot CHBr\cdot CHBr\cdot CH_2\cdot CHBr\cdot}\underset{\textit{threo-}}{CHBr\cdot[CH_2]_7\cdot CO_2H} \quad \text{(VI)}$$

mμ). The intermediate ethyl linoleate contained approximately 2—3% of *trans*-isomers (estimates based on the intensity of band at 969 cm.$^{-1}$). Small amounts of *trans*-isomers were presumably also present in the linoleic acid but could not be detected as a broad band at 934 cm.$^{-1}$ masked the band at 969 cm.$^{-1}$.

Several syntheses of *cis-cis*-linoleic acid have been described [4] but none gives the *cis-trans*-isomers. The conversion of the enynamide (II; $n = 7$) into these isomers is therefore being examined.

Experimental

Ultraviolet spectra were measured on a Unicam S.P. 700 recording spectrophotometer.

trans-NN-*Dimethylnonadec-13-en-10-ynamide*.—Sodamide (3·9 g.) was stirred with liquid ammonia (*ca.* 300 c.c.) and *NN*-dimethylundec-10-ynamide [1] (21 g.) in ether (50 c.c.) was added during 5 min. Oct-2-enyl bromide [5] (19 g.) was added and the mixture was refluxed for 5 hr. and then allowed to evaporate. After addition of dilute hydrochloric acid, the product was isolated with ethyl acetate; repeated fractional distillation gave the *enynamide* (6·5 g.), b. p. 187—190°/0·4 mm., n_D^{20} 1·4819 (Found: C, 78·3; H, 12·0; N, 4·4. $C_{21}H_{37}NO$ requires C, 78·9; H, 11·7; N, 4·4%), $\nu_{max.}$ 1646 ((CO·NMe$_2$) and 971 cm.$^{-1}$ (*trans*-CH=CH–). There was no band at about 995 cm.$^{-1}$ (–CH=CH$_2$), showing the absence of the alternative product from coupling at the 3-position of the allylic halide.

erythro-13,14-*Dihydroxynonadec-10-ynoic Acid*.—The enynamide (5·8 g.) was treated with 98% formic acid (20 c.c.) and 30% hydrogen peroxide (5 c.c.) at 40°. The mixture was cooled

[2] Huber, *J. Amer. Chem. Soc.*, 1951, **73**, 2730.
[3] Cram and Allinger, *J. Amer. Chem. Soc.*, 1956, **78**, 2522.
[4] *Inter al.*, Raphael and Sondheimer, *J.*, 1950, 2100; Walborsky, Davis, and Howton, *J. Amer. Chem. Soc.*, 1951, **73**, 2590; Gensler and Thomas, *ibid.*, p. 4601; Osbond, Philpott, and Wickens, *J.*, 1961, 2779.
[5] Naves, *Helv. Chim. Acta*, 1943, **26**, 1998.

XUM

to moderate the exothermic reaction and then warmed at 40° for 20 hr., more formic acid (10 c.c.) and hydrogen peroxide (2·5 c.c.) being added after 2 hr. The gum obtained by evaporation *in vacuo* was refluxed for 4 hr. with ethanol (100 c.c.) and 5N-sodium hydroxide (100 c.c.). Acidification, followed by isolation with ethyl acetate, gave the *dihydroxy-acid*, plates, m. p. 99—100° (from ethyl acetate) (Found: C, 69·6; H, 10·0. $C_{19}H_{34}O_4$ requires C, 69·9; H, 10·5%).

8-*Bromo-octanoic Acid*.—6-Bromohexan-1-ol [6] (181 g., 1 mol.) was added to sodiomalonic ester (1·2 mol.) in ethanol (500 c.c.) and the mixture was refluxed for 6 hr. After removal of most of the solvent by distillation, dilute sulphuric acid was added and the product isolated in benzene. The solvent-free oil was slowly distilled with acetic acid (200 c.c.) and 48% hydrobromic acid (200 c.c.) for 4 hr.; 20N-sulphuric acid (20 c.c.) was added and the mixture was refluxed until decarboxylation was complete. 48% Hydrobromic acid (250 c.c.) and concentrated sulphuric acid (75 c.c.) were added and the mixture was heated at 110° (internal) for a further 7 hr. After addition of water (1250 c.c.) and repeated extraction with carbon tetrachloride, the combined organic layers were washed with 2N-sodium acetate and water, dried (Na_2SO_4), and distilled. The bromo-acid (151 g., 68%), b. p. 149—153°/1·5 mm., had m. p. 34—36°. Chuit and Hausser [7] gave m. p. 38·5—39°.

8-*Bromo*-NN-*dimethyloctanamide*.—The bromo-acid (151 g.) was warmed with thionyl chloride (180 c.c.) at 30° for 1 hr. and then at 100° for 2 hr. After removal of excess of thionyl chloride, dimethylamine was passed into an ice-cooled, stirred solution of the acid chloride in ether (200 c.c.) until the exothermic reaction ceased. The mixture was washed with water, 2N-sulphuric acid, 2N-sodium carbonate, and water, dried (Na_2SO_4), and evaporated. The *amide* was a yellow oil (142 g.), b. p. 133—136°/0·8 mm., n_D^{20} 1·4920 (Found: C, 48·0; H, 8·1; N, 5·2. $C_{10}H_{20}BrNO$ requires C, 48·0; H, 8·0; N, 5·6%).

NN-*Dimethyldec*-9-*ynamide*.—Acetylene was passed into a stirred suspension of sodamide (25 g.) in liquid ammonia (700 c.c.) and tetrahydrofuran (700 c.c.) for 1·5 hr. The bromo-amide (122 g.) in tetrahydrofuran (250 c.c.) was added and the mixture was refluxed for 5 hr. and then allowed to evaporate. Addition of water and isolation with ether yielded the acetylenic *amide* which was distilled through a short Fenske column. This product (79 g.) had b. p. 103—105°/0·15 mm. and solidified as large prisms, f. p. 25° (thermometer in liquid) (Found: C, 74·1; H, 11·2; N, 7·0. $C_{12}H_{21}NO$ requires C, 73·8; H, 10·8; N, 7·2%).

trans-NN-*Dimethyloctadec*-12-*en*-9-*ynamide*.—*NN*-Dimethyldec-9-ynamide (25·4 g.) in dry tetrahydrofuran (150 c.c.) was added to a stirred suspension of sodamide (5·1 g.) in liquid ammonia (250 c.c.). After 1 hr., oct-2-enyl bromide (32·9 g.) in tetrahydrofuran (50 c.c.) was added and the mixture was stirred under reflux for 5 hr. When the ammonia had evaporated, the product was isolated in the usual manner. The *enynamide* (20 g.) distilled as a pale yellow oil, b. p. 175—177°/0·15 mm., n_D^{20} 1·4812 (Found: C, 78·2; H, 11·6; N, 4·3. $C_{20}H_{35}NO$ requires C, 78·6; H, 11·5; N, 4·6%).

erythro-12,13-*Dihydroxyoctadec*-9-*ynoic Acid*.—The enynamide (50·5 g.) in chloroform (190 c.c.) was treated with 380 c.c. of 0·52M-perbenzoic acid in chloroform at 0°. After 18 hr., 1 mol. of per-acid had been consumed; the solution was washed with 2N-sodium carbonate and water and evaporated. After the addition of 98% formic acid (100 c.c.) the solution was refluxed for 1 hr. and then evaporated *in vacuo*. The residual oil was refluxed with potassium hydroxide (60 g.) in water (60 c.c.) and 2-methoxyethanol (600 c.c.) under nitrogen for 14 hr. Water (100 c.c.) was added and solvent (350 c.c.) was removed by distillation. The hot solution was acidified with acetic acid and then poured into ice–dilute sulphuric acid. erythro-12,13-*Dihydroxyoctadec*-9-*ynoic acid* (20 g.), prisms, m. p. 93·5—94·5°, was obtained by filtration and recrystallisation from methanol (Found: C, 69·0; H, 10·7. $C_{18}H_{32}O_4$ requires C, 69·2; H, 10·3%).

erythro-12,13-*Dihydroxyoctadecanoic Acid*.—The acetylenic acid (250 mg.) in ethanol (50 c.c.) was hydrogenated over 5% palladised charcoal (100 mg.). Filtration and evaporation gave the dihydroxy-acid, prisms (from methanol), m. p. 117—118° (Found: C, 68·5; H, 11·3. Calc. for $C_{18}H_{36}O_4$: C, 68·3; H, 11·5%). Huber [3] gives m. p. 119—120°

erythro-cis-12,13-*Dihydroxyoctadec*-9-*enoic Acid*.—*erythro*-12,13-Dihydroxyoctadec-9-ynoic acid (4·0 g.) in methanol (80 c.c.) was hydrogenated over 5% palladised barium sulphate (0·2 g.) in the presence of quinoline (0·2 g.).[3] The rate of absorption fell sharply when about 0·98 mol. of hydrogen had been taken up; hydrogenation was then interrupted and the filtered

[6] Degering and Boatright, *J. Amer. Chem. Soc.*, 1950, **72**, 5137.
[7] Chuit and Hausser, *Helv. Chim. Acta*, 1929, **12**, 466.

solution was evaporated. Recrystallisation from methanol gave erythro-cis-12,13-*dihydroxyoctadec*-9-*enoic acid* (3·1 g.), prisms, m. p. 76—77·5° (Found: C, 69·1; H, 11·0. $C_{18}H_{34}O_4$ requires C, 68·8; H, 10·9%). This compound was mentioned by Reinger [8] who did not report the m. p. Barucha and Gunstone [9] described an optically active form, m. p. 87—88°.

threo-threo-9,10,12,13-*Tetrabromooctadecanoic Acid*.—Bromine in chloroform (358 c.c. of 0·406N-solution) was added dropwise to the olefinic acid (22·8 g.) in chloroform (700 c.c.) at 20°. The solution was washed with water, dried (Na_2SO_4), and evaporated but the dibromodihydroxy-acid did not crystallise. It was dissolved in hydrogen bromide in acetic acid (344 c.c.; *d* 1·3) and concentrated sulphuric acid (86 c.c.). Next day the solution was warmed to 100° during 1 hr. and kept at 100° for 7 hr., more hydrogen bromide–acetic acid (86 c.c.) being added after 3 hr. The cooled solution was poured into water (2 l.) and extracted with 1 : 1 ether–light petroleum (b. p. 40—60°). Evaporation of the washed and dried extracts gave oil containing some solid, which was recrystallised from ethylene dichloride. The tetrabromo-acid (8·5 g.) had m. p. 114—115°, undepressed on admixture with a sample prepared from natural linoleic acid.[10]

Ethyl Linoleate.—The tetrabromo-acid (10 g.) was esterified azeotropically with benzene (400 c.c.), ethanol (200 c.c.), and concentrated sulphuric acid (1 c.c.). The ester (9 g.), isolated in the usual manner, had m. p. 58—59°. Palmer and Wright [11] give m. p. 58—58·5°.

Zinc dust (15 g.) was heated with ethanol (150 c.c.) to the b. p. and 48% hydrobromic acid (0·1 c.c.) was added. After the mixture had been refluxed under nitrogen for 5 min., the bromo-ester (9·0 g.) in ethanol (50 c.c.) was added slowly and the mixture was refluxed for 1 hr. The zinc was collected and washed with light petroleum; after the combined filtrates had been poured into dilute sulphuric acid, the separated organic layer was washed with water, dried (Na_2SO_4), and distilled under nitrogen. Ethyl linoleate (3·6 g.) thus obtained had b. p. 156°/0·5 mm., n_D^{23} 1·4581 [Found: C, 78·2; H, 11·7%; I val. (Wijs 30 min.), 162·2. Calc. for $C_{20}H_{36}O_2$: C, 77·9; H, 11·8%]. It showed $\lambda_{max.}$ 235 (ε 48) and 278 mμ (ε 11) and a weak band at 969 cm.$^{-1}$ corresponding to 2—3% of *trans*-isomers.

Linoleic Acid.—The ester (3·6 g.) was dissolved in 5% ethanolic sodium hydroxide (50 c.c.) under argon and left overnight at room temperature. After addition of warm water (100 c.c.), the solution was washed with ether, and the aqueous layer was acidified with dilute sulphuric acid. Isolated with ether, the linoleic acid was distilled under argon; it (2·3 g.) had b. p. 177°/0·5 mm., n_D^{23} 1·4672, m. p. −6° to −6·5° (capillary) [Found: C, 77·4; H, 11·5%; *I* val. (Wijs, 30 min.), 179·4. Calc. for $C_{18}H_{32}O_2$: C, 77·1; H, 11·5%]. It showed $\lambda_{max.}$ 238 (ε 15·0) and 270 mμ (ε 18·2). The infrared spectra of both acid and ester were superimposable on those of specimens obtained from natural sources.

We are indebted to Drs. R. E. Bowman and J. F. McGhie for helpful discussions, to Miss E. M. Tanner for spectroscopic data, and to Mr. F. Oliver for microanalyses.

Chelsea College of Science and Technology,
Manresa Rd., London, S.W.3.
Parke Davis & Co., Ltd., Staines Rd.,
Hounslow, Middlesex.

[*Received, June 9th,* 1961.]

[8] Reinger, *Ber. Pharm. Ges.*, 1922, **32**, 124.
[9] Bharucha and Gunstone, *J.*, 1956, 1611.
[10] McCutcheon, *Org. Synth.*, Coll. Vol. III, p. 526.
[11] Palmer and Wright, *J. Ind. Eng. Chem.*, 1914, **6**, 822.

XUM

869. *Pteridine Studies. Part XIV.*[1] *Methylation of 2-Amino-4-hydroxypteridine and Related Compounds.*

By D. J. Brown and N. W. Jacobsen.

2-Amino-4-hydroxypteridine is shown to undergo an unprecedented transannular methylation on $N_{(8)}$, confirmed by an unambiguous synthesis of the product. 4-Amino-2-hydroxypteridine, however, forms a 1-methyl derivative, whose structure is proved by alkaline degradation to 3-methylaminopyrazine-2-carboxylic acid. 2,4-Diaminopteridine gives a mixture of 1- and 8-methyl derivatives.

pK_a values and ultraviolet spectra of the products and related compounds indicate that the predominant tautomer of " 2-amino-4-hydroxypteridine " (the fundamental unit of naturally occurring pteridines) is 2-amino-3,4-dihydro-4-oxopteridine, and that the isomeric " 4-amino-2-hydroxypteridine " is probably in the form of 4-amino-1,2-dihydro-2-oxopteridine. Application of Jones's rule suggests that the 1-methyl derivative of 2,4-diamino-6,7-dimethylpteridine exists largely as the tautomer, 4-amino-1,2-dihydro-2-imino-1,6,7-trimethylpteridine.

4-Aminopteridine is readily converted by methyl iodide into 1,4-dihydro-4-imino-1-methylpteridine [2] but attempts to isolate a product on methylation of 2-aminopteridine have so far failed. However, 4-amino-2-hydroxy-, 2-amino-4-hydroxy-, and 2,4-diaminopteridines proved more amenable to such treatment.

4-Amino-2-hydroxypteridine gave a single monomethyl derivative which was shown to be 4-amino-1,2-dihydro-1-methyl-2-oxopteridine (I; R = Me) by alkaline degradation to 1-methyl-lumazine [3] (II; R = H) and to 3-methylaminopyrazine-2-carboxylic acid (III; R = OH). The structure of the pyrazine was proved by preparation from its known [4] amide (III; R = NH_2). 4-Amino-2-hydroxy-6,7-dimethylpteridine (prepared from 4,5,6-triamino-2-hydroxypyrimidine and biacetyl), when methylated similarly, gave the 6,7-dimethyl derivative of (I), the structure of this being confirmed by alkaline hydrolysis to 1,6,7-trimethyl-lumazine [5] (II; R = Me) and then to the known [2] 5,6-dimethyl-3-methylaminopyrazine-2-carboxylic acid.

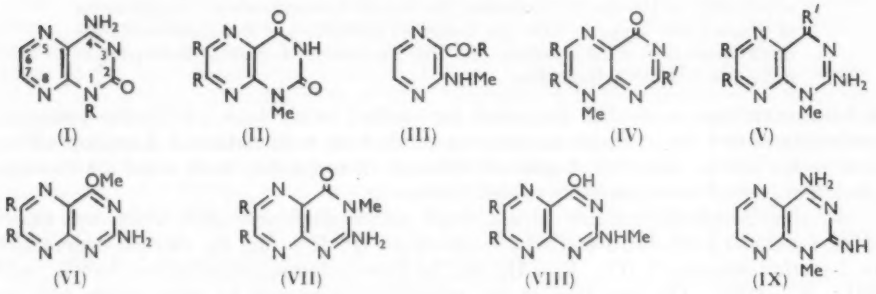
As in the above cases, other amino- and hydroxy-pteridines have always been methylated only in the ring bearing the substituents. Thus 4-methylamino-,[2] and 2- [4] and 4-hydroxypteridine give 1-methyl derivatives though the last gives also an *O*- and a 3-methyl derivative; 6- and 7-hydroxy- and 6,7-dihydroxy-pteridine [4] give, respectively, 5- and 8-methyl and 5,8-dimethyl derivatives. It was, therefore, unexpected that 2-amino-4-hydroxypteridine should undergo transannular methylation, yielding exclusively 2-amino-4,8-dihydro-8-methyl-4-oxopteridine (IV; R = H; R′ = NH_2). The 8-alkylated pteridines found in Nature [6] may arise in this way. The structure of the product was shown as follows.

Because methylation at position 5 is precluded by valency, there are five possible structures (V; R = H, R′ = O), (VI—VIII; R = H), and (IV; R = H, R′ = NH_2). The first of these compounds was synthesised in another connexion (see below); 2-amino-4-methoxypteridine and 2-amino-3,4-dihydro-3-methyl-4-oxopteridine were prepared from pyrimidine precursors [7,8] by processes more simple than those recently described; [9] and

[1] Part XIII, *J.*, 1961, 127.
[2] Brown and Jacobsen, *J.*, 1960, 1978.
[3] Pfleiderer, *Chem. Ber.*, 1957, **90**, 2582.
[4] Albert, Brown, and Wood, *J.*, 1956, 2066.
[5] Sachs and Meyerheim, *Ber.*, 1908, **41**, 3957.
[6] Masuda, Kishi, Asai, and Kuwada, *Chem. and Pharm. Bull.*, 1959, **7**, 366; Taylor and Loux, *J. Amer. Chem. Soc.*, 1959, **81**, 2474.
[7] Roth, Smith, and Hultquist, *J. Amer. Chem. Soc.*, 1951, **73**, 2864, 2869.
[8] Curran and Angier, *J. Amer. Chem. Soc.*, 1958, **80**, 6095.
[9] Pfleiderer, Liedek, Lohrmann, and Rukwied, *Chem. Ber.*, 1960, **93**, 2015.

4-hydroxy-2-methylaminopteridine was made by a new route from 4-amino-6-hydroxy-2-methylaminopyrimidine by nitration, reduction to the 4,5-diamino-analogue, and condensation with glyoxal. None of these substances resembled the methylation product of 2-amino-4-hydroxypteridine, but the remaining isomer, 2-amino-4,8-dihydro-8-methyl-4-oxopteridine (made from 2,5-diamino-4-hydroxy-6-methylaminopyrimidine [10] and glyoxal) proved identical with it (compared as hydrochlorides).

It seemed wise to confirm this with the 6,7-dimethyl homologues. 2-Amino-4-hydroxy-6,7-dimethylpteridine gave a single methyl derivative similar in spectra and pK_a values to the previous product (IV; R = H; R′ = NH_2). Identity with four of the five possible isomers, (V; R = Me, R′ = O) and (VI—VIII; R = Me), can be eliminated by their published constants.[7,8] The fifth isomer [10] (IV; R = Me, R′ = NH_2) proved, on comparison of hydrochlorides, to be identical with the methylation product, confirming that 8-alkylation had again taken place.



2,4-Diaminopteridine gave two methyl derivatives. As already reported,[11] and although it has not been obtained pure, one of these has structure (IX) or (V; R = H, R′ = NH), as shown by the following degradation of impure material. With ice-cold sodium hydroxide solution it rapidly gave 2-amino-1,4-dihydro-1-methyl-4-oxopteridine (V; R = H, R′ = O) which on brief hydrolysis in warm alkali gave 1-methyl-lumazine (II; R = H). This in turn was degraded by prolonged hydrolysis to the acid (III; R = OH), which had been synthesised unambiguously as mentioned above. The possibility that the initial hydrolysis product has the 4-amino-structure (I; R = Me) rather than (V; R = H, R′ = O) is excluded by synthesis and confirmation of the structure of the former (see above), as well as by a recent unambiguous synthesis [9] of the latter. The formation of the 1-methyl derivative (IX) parallels that of its 6,7-diphenyl derivative reported by Boon and Bratt.[12]

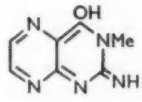
The second methylated product was obtained pure. It was not degraded by alkali and its spectrum differed from that of 4-amino-1,2-dihydro-2-imino-1,6,7-trimethylpteridine and 2,4-diaminopteridine (see Table). This precludes its being the 1-methyl derivative (IX) or 2-amino-4-methylamino- or 4-amino-2-methylamino-pteridine (the last two would resemble 2,4-diaminopteridine spectrographically). Of the remaining possibilities the 8-methylated derivative is strongly suggested by the extraordinarily long-wavelength absorption, typical of transannularly methylated imino- and oxo-pteridines shown in the Table and elsewhere.[2,10,13-15] This is confirmed by the similarity of the spectrum of its neutral molecule to that of the anion of 2-amino-4,8-dihydro-8-methyl-4-oxopteridine, as

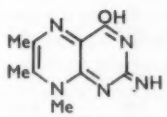
[10] Fidler and Wood, *J.*, 1957, 4157.
[11] Brown and Jacobsen, *Tetrahedron Letters*, 1960, No. 25, p. 17.
[12] Boon and Bratt, *J.*, 1957, 2159.
[13] Brown and Mason, *J.*, 1956, **3443**.
[14] Masuda, *Pharm. Bull. (Japan)*, 1957, **5**, 28.
[15] Pfleiderer and Nübel, *Chem. Ber.*, 1960, **93**, 1406.

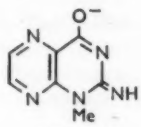
would be expected of the 8-methyl isomer according to the R.N. Jones rule.[16] Moreover, its basic strength (pK_a 8·9) is intermediate between those of the parent pteridine (pK_a 5·3) and its 1,6,7-trimethyl derivative (pK_a 11·9), in line with analogous cases of transannularly methylated iminopteridines.[2,10] Transannular methylation was finally proved by acid hydrolysis in good yield to 2-amino-4,8-dihydro-8-methyl-4-oxopteridine (IV; R = H, R′ = NH_2).

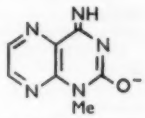
Like its simpler homologue, 2,4-diamino-6,7-dimethylpteridine gave two products on methylation. The major one was degraded by alkali to 1,6,7-trimethyl-lumazine [5] (II; R = Me) and is therefore the 1-methyl derivative. The minor product could not be obtained entirely free from the major one but analysis of the mixture indicated that the constituents are isomeric, and by analogy it is assumed to be the 8-methyl derivative.

The Table shows that the amino-hydroxypteridines methylated on O, $N_{(1)}$, $N_{(3)}$, or the extranuclear N-atom, are quite weak bases, of pK_a <3·5, indistinguisable in this respect from their unmethylated precursors. This indicates that the preferred tautomeric form in these cases involves an amino-form (as in VII) rather than an imino-form (as in X), which must be more strongly basic.[2,17] On the other hand, $N_{(1)}$-methylated 2,4-diamino-6,7-dimethyl-pteridine, which must involve an imine as (IX) or (V; R = Me, R′ = NH), is an exceptionally strong base of pK_a *ca.* 12.


(X)


(XI)


(XII)


(XIII)

The basic strengths of 8-methylated 2-amino-4-hydroxypteridines are markedly greater than those of the 1- and 3-methyl isomers. Thus the simple derivative (IV; R = H, R′ = NH_2) has pK_a 5·4, and its 6,7-dimethyl derivative has pK_a 6·1. That the basic strength of the latter approximates to that of 2,8-dihydro-2-imino-6,7,8-trimethylpteridine (5·6) led Fidler and Wood [10] to postulate the hydroxy-imino-structure (XI) for the compound, and a pK_a of 8·9 was assigned to the hydroxy-group. We have been unable to confirm the latter constant, but find an anionic pK_a 12, which is more in line with those of the 1- and 3-methyl analogues that are forced into an hydroxy-imino-form such as (XII) only at high pH values. The recorded value of 8·9 may have arisen from the formation of 6,7,8-trimethyl-lumazine (pK_a 9·8) by partial hydrolysis of the amino-group during measurement. Moreover, the enhanced basic strength of compound (IV; R = Me, R′ = NH_2) is in line with that of 4,8-dihydro-6,7,8-trimethyl-4-oxopteridine [13] (IV; R = Me, R′ = H), which can involve no imine but has a comparably enhanced basic strength (pK_a 4·7) when compared with the isomeric 1,4-dihydro-1,6,7-trimethyl-4-oxopteridine [2] (pK_a 1·7). It is, therefore unwarranted, in the face of accepted general principles,[17] to assume the hydroxy-imino-form (XI) at the expense of the usual amino-oxo-forms (IV; R = H or Me, R′ = NH_2).

It is of special interest to discover the preferred tautomeric form of 2-amino-4-hydroxypteridine in aqueous solution because this structure is common to almost all of the natural pteridines. Valency permits this substance to exist in 9 forms. The five imino-forms (three hydroxy-imino-tautomers with the mobile hydrogen atom severally at positions 1, 3, and 8, as well as two imino-oxo-tautomers each with two hydrogen atoms at positions 1,3 and 1,8) are precluded by the weakly basic nature of 2-amino-4-hydroxypteridine (pK_a 2·3) because all known pteridine and related imines are much stronger bases.[2,10]

[16] Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127.
[17] Brown, Hoerger, and Mason, *J.*, 1955, 4035; Angyal and Angyal, *J.*, 1952, 1461; Albert, "Heterocyclic Chemistry," Athlone Press, London, 1959, pp. 54 *et seq.*

This has been confirmed by the marked similarity in spectra [9] of 2-amino-4-hydroxy- and 4-hydroxy-2-dimethylamino-pteridine, the second of which cannot assume an imino-form. A similar conclusion can be drawn from a comparison of their 6,7-dimethyl derivatives.[7]

Compound	pK_a [a] and concn.	$\lambda_{max.}$ (mμ) [b]	pH	log ε
Pteridine derivatives				
4-Amino-1,2-dihydro-1-methyl-2-oxo		345; 288; 245	5·0	3·88; 3·56; 4·13
cation	2·96 ± 0·02 (M/400)	*360*; 341; 238	0·13	*3·68*; 3·87; 4·08
anion	*ca.* 12	350; 245	14·0	3·79; 4·04
4-Amino-1,2-dihydro-1,6,7-trimethyl-2-oxo		*360*; 345; 282; 248; 216	7·1	*3·93*; 4·04; 3·53; 4·24; 4·18
cation	3·66 ± 0·03 [c]	360; 343; *264*; 218	0·3	3·91; 4·02; *3·82*; 4·29
4-Amino-2-hydroxy		*350*; 337; *286*; 240	7·0	*3·87*; 3·94; *3·63*; 4·08
cation	2·99 ± 0·02 [c, d]	335; 237	0·83	3·90; 4·08
anion	9·97 [e]	375; 255	12·0	3·85; 4·31
2-Amino-1,4-dihydro-1-methyl-4-oxo		See Figure	5·0	
cation	2·83 ± 0·03 (M/200)	—[f]	—	—
anion	*ca.* 11·5	360; 258	14·0	3·90; 4·13
2-Amino-3,4-dihydro-3-methyl-4-oxo		See Figure	5·0	—
cation	2·25 ± 0·03 [c]	—[f]	—	—
2-Amino-4,8-dihydro-8-methyl-4-oxo		400; 320; 265	8·5	3·98; 3·47; 4·28
cation	5·42 ± 0·02 (M/200)	389; *283*; 261	3·0	4·01; *3·99*; 4·14
anion	*ca.* 11·5	314; 284; 239	14·0	3·91; 3·89; 4·26
2-Amino-4,8-dihydro-6,7,8-trimethyl-4-oxo		407; 315; 267	8·5	4·11; 3·43; 4·35
cation	6·10 ± 0·02 (M/200) [g]	397; 285; 254	3·0	4·12; 4·13; 4·09
anion	11·97 ± 0·02 [c]	370; 308; *301*; 228 [h]	14·0	3·88; 4·20; *4·18*; 4·33
2-Amino-4-hydroxy [e]		See Figure	5·25	
cation	2·31	315; <220		3·88; >4·1
anion	7·92	358; 251		3·83; 4·31
4-Amino-2-hydroxy-6,7-dimethyl		*350*; 340; 276; 245	6·5	*3·96*; 4·01; 3·48; 4·07
cation	3·49 ± 0·03 [c]	*350*; 338; *256*; 215	1·3	*3·97*; 4·03; *3·85*; 4·32
anion	10·69 ± 0·04	370; *274*; 254	13·8	3·88; *3·78*; 4·29
4-Amino-2,8-dihydro-2-imino-8-methyl [i]		*365*; 313; 288; 241	11·0	*3·23*; 3·92; 3·93; 4·11
cation	8·88 ± 0·04 [c]	412; 330; 270; *244*	6·0	3·98; 3·52; 4·24; *3·73*
4-Amino-1,2-dihydro-2-imino-1,6,7-trimethyl		368; 262	14·16	3·97; 4·15
cation	11·90 ± 0·05 [c]	*347*; 335; 282; *246*	7·5	*4·01*; 4·07; 3·64; *4·25*
2,4-Diamino		364; 255; 224	8·0	3·86; 4·32; 4·07
cation	5·32 [e]	*345*; 332; *318*; 284; 240	3·0	*3·90*; 3·98; *3·91*; 3·73; 4·10
1-Methyl-lumazine, anion [k]	8·57 ± 0·02 (M/200)	339; 281; 242	10·5	3·89; 3·54; 4·19
3-Methyl-lumazine, anion [k]	8·0	362; 268; 244; 215	10·0	3·81; 3·98; 4·25; 4·02
1,6,7-Trimethyl-lumazine		334; 252; *225*	7·0	3·98; 3·96; 4·07
anion	9·06 ± 0·04 (M/300)	341; *280*; 244	11·5	4·03; *3·38*; 4·25
6,7,8-Trimethyl-lumazine		404; 276; 256	7·0	4·08; 4·04; 4·16
anion	9·83 ± 0·04 (M/400)	363; 313; *304*; 243	12·0	3·78; 4·31; *4·28*; 4·19
Lumazine, dianion [m]		365; 252		3·78; 4·23

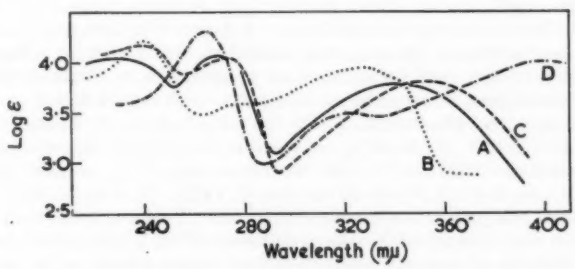
[a] By potentiometric titration in water at 20° (cf. Albert and Phillips, *J.*, 1956, 1294). For values for other compounds see Experimental section. [b] Inflexions in italics. [c] Spectrometrically determined. [d] Cf. approx. value of 3·2 by potentiometric titration, ref. 19. [e] From ref. 19. [f] For spectrum see ref. 9. [g] Cf. 5·85 given in ref. 10. [h] The peak at 268 mμ recorded by Fidler and Wood (ref. 10) at pH 13 arises from that of the neutral molecule, present to the extent of 10% in their solution. [i] Constants measured on dihydriodide with balanced I^- concentration in reference cell. [k] Spectrum from ref. 3. [l] Prep.: ref. 14 and Birch and Moye, *J.*, 1958, 2622; values determined on supplied specimens; cf. pK_a 9·86 in ref. 15. [m] Values from Albert, Brown, and Cheeseman, *J.*, 1951, 474.

The one possible amino-hydroxy-form can also be eliminated by dissimilarity in spectra [9] between 2-amino-4-hydroxy- and 2-amino-4-methoxy-pteridine. There remain the three amino-oxo-forms with hydrogen located severally at positions 1, 3, and 8. Comparison of the spectrum of 2-amino-4-hydroxypteridine as neutral molecule with those of its 1-, 3-, and 8-methyl derivatives (see Figure) leaves little doubt that the hydrogen occupies position 3 and that 2-amino-3,4-dihydro-4-oxopteridine is the predominant tautomer, at least in aqueous solution, as believed also by Pfleiderer *et al.*[9] This stands in contrast to its methylation at position 8 and its reported protonation [9] at position 1, but is in line with the recorded preference [13,18] for an α-cyclic amide at the expense of a γ-vinylogous cyclic amide where the choice exists in 1,3-diazines.

Similar treatment cannot be accorded to 4-amino-2-hydroxypteridine because the range of methylated reference compounds is incomplete. However, its weak basic strength and the close similarity of its spectrum (neutral molecule) to that of 4-amino-1,2-dihydro-1-methyl-2-oxopteridine (1; R = Me) suggests that (unlike its isomer) it carries a hydrogen atom at position 1, the principal tautomer being 4-amino-1,2-dihydro-2-oxopteridine (I; R = H).

The spectrum of the neutral molecule of 4-amino-1,2-dihydro-2-imino-1,6,7-trimethylpteridine reveals the compound's tautomeric form. If allowance is made for the usual small bathochromic shift resulting from the *C*-methyl groups, the spectrum approximates more closely to that of the anion of 2-amino-1,4-dihydro-1-methyl-4-oxopteridine (XII) than to that of the anion of 4-amino-1,2-dihydro-1-methyl-2-oxopteridine (XIII). Application of Jones's rule [16] (that the spectrum of an amino-derivative is similar to that of the anion of the corresponding hydroxy-derivative) suggests that the methylated diamine

Absorption, as neutral molecules, of: A, 2-*amino*-4-*hydroxypteridine*; B, 2-*amino*-1,4-*dihydro*-1-*methyl*-4-*oxopteridine*; C, 2-*amino*-3,4-*dihydro*-3-*methyl*-4-*oxopteridine*; D, 2-*amino*-4,8-*dihydro*-8-*methyl*-4-*oxopteridine*.



is probably best represented as 4-amino-1,2-dihydro-2-imino-1,6,7-trimethylpteridine. Simple examples supporting the validity of the rule in this series are the similarity of the spectra of 2,4-diaminopteridine (neutral molecule) to those of the anions of 4-amino-2-hydroxy- and 2-amino-4-hydroxy-pteridine and the dianion of lumazine (see Table).

Experimental

Analyses were done by Dr. J. E. Fildes and staff.

3-Methylaminopyrazine-2-carboxylic Acid.—1,4-Dihydro-1-methyl-4-methyliminopteridine hydrochloride [2] (0·45 g.) was stirred in N-sodium hydroxide (10 ml.) at 100° for 2·5 hr. The solution was adjusted to pH 1 with hydrochloric acid and evaporated to dryness. The powdered residue was extracted with boiling benzene (2 × 20 ml.), and the solid obtained on evaporation was recrystallized from water (50 parts) to give the *pyrazine* (72%), m. p. 182° (decomp.) (Found: C, 47·0; H, 4·5; N, 27·4. $C_6H_7N_3O_2$ requires C, 47·05; H, 4·6; N, 27·4%). The same product

[18] Brown, Hoerger, and Mason, *J.*, 1955, 211; Brown and Mason, *J.*, 1957, 682.

was obtained similarly from 1,4-dihydro-4-imino-1-methylpteridine [3] and from 3-methylaminopyrazine-2-carboxamide.[4]

4-Amino-1,2-dihydro-1-methyl-2-oxopteridine.—4-Amino-2-hydroxypteridine [19,20] (1·35 g.), methyl iodide (5·2 ml.), and methanolic sodium methoxide (200 ml.; from sodium, 0·21 g.) were refluxed for 1 hr. Recrystallization of the solid from water (160 parts) gave the *methyl-pteridine* (75%), m. p. 324—325° (decomp.) (Found: C, 47·6; H, 4·0; N, 39·4. $C_7H_7N_5O$ requires C, 47·45; H, 4·0; N, 39·5%).

This pteridine (0·3 g.) was stirred in N-sodium hydroxide (15 ml.) for 5 hr. at 100°. The solution was adjusted to pH 1 and evaporated to dryness, and the residue continuously extracted with benzene. The extract was taken to dryness and sublimed at 120°/0·02 mm. to give 3-methylaminopyrazine-2-carboxylic acid (39%), m. p. and mixed m. p. 180°. The unsublimed part (30%), when recrystallized from ethanol and sublimed (220°/0·02 mm.), had m. p. 285°, undepressed on admixture with 1-methyl-lumazine.

4-Amino-1,2-dihydro-1,6,7-trimethyl-2-oxopteridine.—4,5,6-Triamino-2-hydroxypyrimidine sulphate [21] (4·8 g.) and sodium hydrogen carbonate (3·4 g.) in water (350 ml.) were stirred on the steam-bath with biacetyl (1·8 g.) for 15 min. The resulting solid (3·4 g.) dissolved in hot water (150 parts) on addition of hydrochloric acid to pH 2·5, and the *4-amino-2-hydroxy-6,7-dimethylpteridine*, m. p. *ca.* 340° (decomp.), crystallized on slow addition of sodium acetate to pH 5 (Found: C, 50·3; H, 4·75; N, 36·15. $C_8H_9N_5O$ requires C, 50·25; H, 4·7; N, 36·6%).

This pteridine (1 g.) and methyl iodide (2·5 ml.) were refluxed for 1 hr. in methanolic sodium methoxide (25 ml.; from sodium, 0·13 g.). After chilling, the water-washed solid (84%) recrystallized from ethanol (350 parts), to give the *trimethyloxopteridine*, m. p. 314—316° (decomp.) (Found: C, 52·65; H, 5·4; N, 33·7. $C_9H_{11}N_5O$ requires C, 52·65; H, 5·4; N, 34·1%). Hydrolysis in boiling N-sodium hydroxide (25 parts) for 15 min. gave, after adjustment to pH 5, 1,6,7-trimethyl-lumazine (83%), m. p. 328—330° (lit.,[5] 328—330°) (Found: C, 52·5; H, 4·8; N, 27·15. Calc. for $C_9H_{10}N_4O_2$: C, 52·4; H, 4·9; N, 27·15%). This substance (0·42 g.) was further heated with 2·5N-sodium hydroxide (16 ml.) at 200° for 4 hr. After treatment with charcoal and evaporation, the residue recrystallized from light petroleum (b. p. 60—80°; 165 parts) to give 5,6-dimethyl-3-methylaminopyrazine-2-carboxylic acid (35%), m. p. and mixed m. p. (ref. 2) 143—145°.

2-Amino-4,8-dihydro-8-methyl-4-oxopteridine.—2-Amino-4-hydroxypteridine (2 g.), methyl iodide (15 ml.), and methanol (60 ml.) were rocked at 110° for 12 hr. The tube was opened at −40° (dimethyl ether!), and the solution on evaporation to 15 ml. deposited red crystals (1·3 g.). Recrystallization from methanol (140 parts) with concentration gave the *oxopteridine hydriodide*, (decomp.) 265° (Found: C, 27·85; H, 2·8; I, 41·1; N, 22·55. $C_7H_8IN_5O$ requires C, 27·55; H, 2·65; I, 41·6; N, 22·95%). Treatment with silver chloride furnished the *hydrochloride* (from methanol, 330 parts, with concentration), m. p. *ca.* 285° (decomp.) (Found: C, 39·35; H, 3·9; N, 32·7. $C_7H_8ClN_5O$ requires C, 39·35; H, 3·8; N, 32·8%).

This pteridine was also made unambiguously. 2-Amino-4-hydroxy-6-methylamino-5-nitrosopyrimidine was reduced with sodium dithionite [19] or hydrogenated over Raney nickel. An equivalent amount of aqueous hydrochloric acid was added to the crude base (0·9 g.), suspended in methanol (10 ml.). Addition of ether (10 ml.) precipitated *2,5-diamino-4-hydroxy-6-methylaminopyrimidine hydrochloride* (85%), which, recrystallized from methanol, had m. p. 237—238° (decomp.) (Found: C, 31·4; H, 5·5; Cl, 18·25. $C_5H_{10}ClN_5O$ requires C, 31·35; H, 5·25; Cl, 18·5%). This hydrochloride (0·45 g.) was refluxed for 30 min. with polyglyoxal (0·14 g.) in methanol (30 ml.); evaporation to 10 ml. then gave a solid (50%) which after recrystallization was identified with the pteridine hydrochloride by mixed m. p., chromatography in six systems, and infrared spectroscopy.

2-Amino-4,8-dihydro-6,7,8-trimethyl-4-oxopteridine.—2-Amino-4-hydroxy-6,7-dimethylpteridine [22] (1·0 g.) was rocked for 5 hr. at 100° with methyl iodide (7·5 ml.) and methanol (30 ml.). Evaporation and recrystallization from methyl iodide–methanol (35 : 65) gave the *oxopteridine hydriodide* (60%), m. p. 265—270° (decomp.) (Found: C, 32·45; H, 3·5; I, 37·75; N, 20·85. $C_9H_{12}IN_5O$ requires C, 32·45; H, 3·6; I, 38·1; N, 21·0%). Silver chloride converted it into the *hydrochloride* which, recrystallized from 25% aqueous ethanol (26 parts), had m. p. 255—260° (decomp.) (Found: Cl, 14·8; N, 28·75. $C_9H_{12}ClN_5O$ requires Cl, 14·7%; N, 29·0%).

[19] Albert, Brown, and Cheeseman, *J.*, 1952, 4219.
[20] Taylor and Cain, *J. Amer. Chem. Soc.*, 1949, **71**, 2538.
[21] Bendich, Tinker, and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3109.
[22] Cain, Mallette, and Taylor, *J. Amer. Chem. Soc.*, 1946, **68**, 1996.

XUM

It was also prepared in 93% yield from 2,5-diamino-4-hydroxy-6-methylaminopyrimidine hydrochloride and biacetyl (see homologue above), and the products from both routes were identified by mixed m. p., chromatography, and spectroscopy.

2-Amino-4-methoxypteridine.—2,4,5-Triamino-6-methoxypyrimidine sulphate [7] (0·5 g.) and polyglyoxal (0·11 g.) were refluxed for 1 hr. in methanolic sodium methoxide (from sodium, 0·085 g.). The oily residue obtained on evaporation was triturated with water (5 ml.), and the resulting solid recrystallized from water (25 parts). The aminomethoxypteridine (0·14 g.) had m. p. 204—205° (lit.,[9] 207—209°) and pK_a 3·46 ± 0·02 (M/200; 20°) (Found: C, 47·4; H, 3·85; N, 39·4. Calc. for $C_7H_7N_5O$: C, 47·45; H, 4·0; N, 39·5%).

2-Amino-3,4-dihydro-3-methyl-4-oxopteridine.—2,4,5-Triamino-1,6-dihydro-1-methyl-6-oxopyrimidine hydrochloride [9] (0·5 g.), polyglyoxal (0·15 g.), and methanol (60 ml.) were refluxed for 1 hr. Evaporation to *ca.* 5 ml. gave the oxopteridine (70%) which after recrystallization from glacial acetic acid decomposed at *ca.* 320° (lit.,[9] 322°) (18%) (Found: C, 47·65; H, 4·0; N, 39·35. Calc. for $C_7H_7N_5O$: C, 47·45; H, 4·0; N, 39·5%).

4-Hydroxy-2-methylaminopteridine.—4-Amino-6-hydroxy-2-methylaminopyrimidine [7] (5 g.) was added during 30 min. to stirred nitric acid (*d* 1·5; 20 ml.) at 5—10°. After a further 30 min., the mixture was poured on ice. Washing the solid in boiling water (350 ml.) and recrystallization from water (1500 parts) gave *4-amino-6-hydroxy-2-methylamino-5-nitropyrimidine* (73%), m. p. 348—350° (decomp.) (Found: C, 32·7; H, 3·8. $C_5H_7N_5O_3$ requires C, 32·45; H, 3·8%). This nitro-compound (2·5 g.) was hydrogenated over Raney nickel in methanol (250 ml.), and the catalyst filtered off and washed with hot water (50 ml.). The filtrate and washings were added to N-hydrochloric acid (18 ml.) and evaporated to dryness. Addition of ethanol (30 ml.) to the residue (1·9 g.) in hot water (10 ml.) gave *4,5-diamino-6-hydroxy-2-methylaminopyrimidine hydrochloride*, m. p. 275—277° (decomp.) (Found: C, 31·45; H, 5·5; N, 36·3. $C_5H_{10}ClN_5O$ requires C, 31·35; H, 5·25; N, 36·55%).

The diamine hydrochloride (1 g.) and polyglyoxal (0·3 g.) were refluxed in methanol (125 ml.) for 1 hr. The solid recovered by evaporation was recrystallized by dissolution in hot water (400 parts), addition of hot alcohol (400 parts), and concentration. 4-Hydroxy-2-methylaminopteridine (0·69 g.) decomposed at *ca.* 378° (lit.,[9] >350°) and had pK_a 1·98 ± 0·03 (M/200), and 8·16 ± 0·02 (M/400) (Found: C, 47·3; H, 4·0; N, 39·3. Calc. for $C_7H_7N_5O$: C, 47·45; H, 4·0; N, 39·5%).

4-Amino-2,8-dihydro-2-imino-8-methylpteridine (or Tautomer).—2,4-Diaminopteridine [15] (4 g.), methyl iodide (40 ml.), and methanol (80 ml.) were rocked together at 110° for 1 hr. Evaporation gave a crude solid (8·4 g.) which was extracted with boiling methanol (40 ml.). The residue, twice recrystallized from methanol (160 parts) with concentration, gave the *8-methylpteridine dihydriodide* (0·5 g.) as dark red crystals, m. p. 236—237° (Found: C, 19·5; H, 2·1; I, 58·75. $C_7H_{10}I_2N_6$ requires C, 19·45; H, 2·3; I, 58·75%). The dihydriodide (0·28 g.) was heated at 100° with N-hydrochloric acid (36 ml.) for 30 min. The solution was shaken with silver chloride (*ca.* 2 g.) for 1 hr., then filtered and the filtrate was evaporated *in vacuo* to dryness. The residue was dissolved in water (10 ml.) which was then adjusted to pH 3·5 with 5% ammonia solution and chilled. The solid precipitate (80%) recrystallised from water (80 parts), giving 2-amino-4,8-dihydro-8-methyl-4-oxopteridine hydrochloride, identified with authentic material by mixed m. p., paper chromatography in 4 solvents, and infrared and ultraviolet spectroscopy.

The initial methanol extract and the mother-liquors from the dihydriodide recrystallization gave, on evaporation, a yellow solid consisting of the 8-methylpteridine and its 1-methyl isomer. The mixture (6 g.) was dissolved in 0·5N-sodium hydroxide (125 ml.) and kept at 0° for 15 min. Recrystallization of the precipitate (1 g.) from water gave 2-amino-1,4-dihydro-1-methyl-4-oxopteridine, m. p. 336° (decomp.) (lit.,[9] 335—337°) (Found: C, 47·55; H, 4·0; N, 39·5. Calc. for $C_7H_7N_5O$: C, 47·45; H, 4·0; N, 39·5%). This pteridine (0·5 g.) was refluxed in N-sodium hydroxide (7 ml.) for 15 min. Adjustment to pH 5, followed by sublimation and recrystallization of the solid (0·44 g.) from ethanol (260 parts), gave 1-methyl-lumazine, m. p. 285° (lit.,[3] 290—291°) (Found: C, 46·95; H, 3·4; N, 31·35. Calc. for $C_7H_6N_4O_2$: C, 47·2; H, 3·4; N, 31·45%). The methyl-lumazine was refluxed in N-sodium hydroxide for 3 hr. and the solution then adjusted to pH 1—2. The residue obtained on evaporation was extracted with boiling benzene to give 3-methylaminopyrazine-2-carboxylic acid identical with authentic material.

4-Amino-1,2-dihydro-2-imino-1,6,7-trimethylpteridine (or Tautomer).—*2,4-Diamino-6,7-dimethylpteridine* was prepared according to directions by Mallette *et al.*[23] It was triturated with

[23] Mallette, Taylor, and Cain, *J. Amer. Chem. Soc.*, 1947, **69**, 1814.

dilute aqueous sodium hydroxide, washed with hot water, and recrystallised from dimethylformamide (145 parts) or glacial acetic acid (20 parts). It was then chromatographically homogeneous, and despite failure by older methods [23] it gave a satisfactory analysis for carbon and hydrogen by the " rapid combustion " method in admixture with vanadium pentoxide, and for nitrogen by the Kjeldahl method (sealed tube) (Found: C, 50·75; H, 5·35; N, 43·75. $C_8H_{10}N_6$ requires C, 50·5; H, 5·3; N, 44·2%).

This pteridine (2 g.), methyl iodide (20 ml.), and methanol (40 ml.) were rocked together at 110° for 5 hr. The tube was opened at −40° (dimethyl ether!) and the solid (27%) recrystallized from ethanol (40 parts). The *iminopteridine hydriodide* had m. p. 280—285° (decomp.) (Found: C, 32·5; H, 3·85; I, 38·15; N, 25·2. $C_9H_{13}IN_6$ requires C, 32·55; H, 3·95; I, 38·2; N, 25·3%).

The hydriodide (0·23 g.) was refluxed with N-sodium hydroxide (5 ml.) for 15 min. Adjustment to pH 5 and recrystallization from water (250 parts) then gave 1,6,7-trimethyl-lumazine (92%), m. p. and mixed m. p. 327—329°.

When the methylation mixture was heated for 1 hr. and then treated with ether (60 ml.), a solid (1·3 g.) was precipitated. Paper chromatography revealed that repeated recrystallization was ineffective in separating all the above imine from a yellow isomeric hydriodide (Found ,for the mixture: C, 32·4; H, 3·95; I, 37·65; N, 25·1%).

We thank Professor A. J. Birch and Dr. T. Masuda for supplying specimens, Professor A. Albert for discussions, and Mr. H. Satrapa and Mr. D. Light for assistance, and we acknowledge support of N. W. J. by an University Scholarship.

Department of Medical Chemistry, Australian National University, Canberra. [*Received, February 15th*, 1961.]

---

870. *Maytenone. Part I. Isolation and Structural Studies.*

By A. W. Johnson, T. J. King, and R. J. Martin.

Maytenone is shown to be a bisditerpene, probably formed by the oxidation of a phenolic diterpene, such as ferruginol or totarol, to the corresponding α-hydroxycyclohexadienone, which then dimerises by a Diels–Alder mechanism. Several reactions of maytenone are described including the pyrolytic decomposition to propene and a mixture of a C_{20} and a C_{17} catechol. The former has been identified as 8-isopropylpodocarpane-6,7-diol (6-hydroxytotarol) and the latter as podocarpane-6,7-diol.

The yellow outer root bark of the tree *Maytenus dispermus* is a source of the pigment, pristimerin,[1] which is obtained by counter-current distribution of the light-petroleum extract. Also obtained from this separation is a colourless crystalline material, in about 0·03% overall yield, which we have named maytenone. Analysis established the empirical formula as $C_{10}H_{15}O$ and molecular-weight determinations gave values of 266 (Rast), $2360/n$ (*X*-ray), and 624 ± 25 (thermistor-drop technique;[2] this determination was carried out in the University Chemical Laboratory, Cambridge, by Mr. G. Purdy, whose help we gratefully acknowledge). It is now known for reasons which will subsequently become apparent that the Rast method will give a false result, and the reactions of maytenone are best interpreted in terms of a molecular formula of $C_{40}H_{60}O_4$ (molecular weight 604·6). The significant ultraviolet absorption of maytenone occurs at 251 mμ (log ε 3·91) and there are, *inter al.*, weak absorption maxima in the infrared spectrum at 3478 and 3640, and strong absorption at 1710 and 1680 $cm.^{-1}$. These data are compatible with maytenone's containing two hydroxyl groups, one saturated ketonic grouping, and one αβ-unsaturated ketonic group, and these account for all the oxygen atoms of the

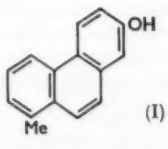
[1] Grant and Johnson, *J.*, 1957, 4079, 4669; Grant, Johnson, Juby, and King, *J.*, 1960, 549.
[2] Iyengar, *Rec. Trav. Chim.*, 1954, **73**, 789.

molecule. Finally, two strong bands of almost equal intensity at 1370 and 1390 cm.$^{-1}$ suggest the presence of at least one *gem*-dimethyl grouping (>CMe_2).

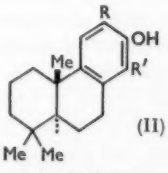
Maytenone is stable to quite vigorous treatment with alkali or aqueous or alcoholic mineral acid, fails to react with periodate, ozone, chromic acid, and the usual ketonic reagents, and is inert to catalytic hydrogenation. Its stability to chromic oxidation suggests that both hydroxyl groups are tertiary, a postulate supported by our inability to acetylate or benzoylate the compound. The presence of one of the ketone groups in maytenone was confirmed when lithium aluminium hydride reduction of an ethereal solution afforded an alcohol, maytenol, $C_{40}H_{62}O_4$, the spectral properties of which were consistent with the reduction of the saturated ketone group. Maytenol was readily acetylated and could be re-oxidised to maytenone. It is assumed that, because of steric reasons, the αβ-unsaturated ketone system is stable in the presence of lithium aluminium hydride under these conditions; other examples of this phenomenon have been reported, *e.g.*, 3-chloro-5,5-dimethylcyclohex-2-enone.[3] More vigorous reduction with lithium aluminium hydride reduced the αβ-unsaturated ketone function as well but the reaction was not always reproducible. The only crystalline compound obtained from the reaction still contained a carbonyl group and the reduction appeared to involve only the conjugated double bond. A similar reduction of the αβ-unsaturated ketone system of 6-oxocativic acid has been reported.[4]

During the attempted acetylation of maytenone with acetic anhydride and perchloric acid, a new compound was obtained, the ultraviolet absorption curve of which was similar to that of maytenone. The positions of the carbonyl bands in the infrared spectrum also corresponded to those of maytenone, but the hydroxyl bands were missing in the spectrum of the new product. This change is best interpreted as a dehydration involving both hydroxyl groups of maytenone to give an ether, anhydromaytenone, $C_{40}H_{58}O_3$, and this view was supported by analysis and by the appearance of a new band in the infrared spectrum at 1050 cm.$^{-1}$, which could be attributed to the presence of the ether grouping. Subsequently the same product was obtained from maytenone by the action of other acidic dehydrating agents, *e.g.*, formic acid and acetic anhydride–toluene-*p*-sulphonic acid. Anhydromaytenone was unaffected by the action of chromic acid or ozone or catalytic hydrogenation.

A relation of maytenone to the diterpenes was indicated by the isolation of a single crystalline product, 8-methyl-2-phenanthrol (I) from dehydrogenation of maytenone with selenium at 320—360°. Distillation of the phenol with zinc gave 1-methylphenanthrene. Dehydrogenation of totarol[5] (II; R = H, R′ = $CHMe_2$) had previously given 8-methyl-2-phenanthrol, and we are indebted to Dr. Wang for an authentic specimen of this compound which was identified with our product. If pristimerin can be regarded as a modified triterpene, then this is one of the rare occasions where di- and tri-terpenes are found in co-existence.[cf. 6]



(I)



(II)

Perhaps the most striking reaction of maytenone is its decomposition on melting. This occurs with the evolution of gas and the formation of a pale yellow resin which distils under reduced pressure without further decomposition. The gas has been shown (vapour-phase chromatography and infrared spectrum) to be very pure propene. This highly

[3] Frank and Hall, *J. Amer. Chem. Soc.*, 1950, **72**, 1645.
[4] Halsall and Moyle, *J.*, 1960, 1324.
[5] Short and Stromberg, *J.*, 1937, 516; Short and Wang, *J.*, 1951, 2979.
[6] Cocker, Halsall, and Bowers, *J.*, 1956, 4259.

specific elimination of propene must have structural significance, especially as the pyrolytic decomposition of maytenol required a higher temperature, *ca.* 270°, and produced propene in smaller yield and accompanied by other gaseous products, *e.g.*, hydrogen, propane, ethylene, and water. Moreover, unlike the decomposition of maytenone, the pyrolysis of maytenol was acid-catalysed, phenols being produced readily at 190° in presence of potassium hydrogen sulphate and even by boiling formic acid. The resin from the pyrolysis of maytenone was phenolic (ultraviolet absorption) and in fact a catechol (green ferric reaction, reduction of pH of boric acid solutions, retardation on borate-treated paper, easy aerial oxidation of an alkaline solution), a conclusion confirmed by silver oxide oxidation of the phenol to an unstable coloured compound which gave a crystalline quinoxaline with *o*-phenylenediamine. Later work showed that the phenolic pyrolysis product was a mixture of two catechols, one of which gave a readily purified crystalline benzoate, the analysis of which indicated that it was derived from a C_{20} dihydric phenol. In view of the production of the methylphenanthrol (I) by dehydrogenation, it seemed that a possible structure for the C_{20} catechol was 8-isopropylpodocarpan-6,7-diol (6-hydroxytotarol) (II; R = OH, R′ = $CHMe_2$). When this compound was synthesised from totarol by nitration, reduction, and diazotisation (following paper) it proved to be identical with the pyrolysis product of maytenone. A quantitative study of the pyrolysis showed that each molecule of maytenone gave only one of propene and suggested that the decomposition was taking the course, $C_{40} \longrightarrow C_{20} + C_3 + C_{17}$; this was confirmed by the yield of the C_{20} dibenzoate. The mother liquors from which the crystalline dibenzoate had separated afforded, after removal of the benzoyl groups with lithium aluminium hydride, another catechol, $C_{17}H_{24}O_2$, which gave an oily dibenzoate but a crystalline di-*p*-nitrobenzoate. It was probable that this catechol was either (II; R = OH, R′ = H) or (II; R = H, R′ = OH) with the former structure favoured because the crude pyrolysis product gave a negative Gibbs test.[7] The catechol (II; R = H, R′ = OH) was first synthesised (following paper) but did not give a crystalline di-*p*-nitrobenzoate. The catechol (II; R = OH, R′ = H) has recently been synthesised (forthcoming publication) and its identity with the pyrolysis product from maytenone has been established.

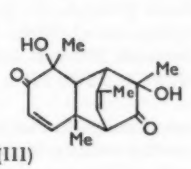
The thermal decomposition of maytenone, which is not catalysed by acid or alkali, suggests that the reaction might be of the reverse Diels–Alder type, in which case the two units making up the maytenone molecule would probably be of the α-hydroxycyclohexadienone type. Such compounds are oxidation products of phenols [8] and are known to be dimerised easily by the Diels–Alder reaction. Thus Adler *et al.*[9] have shown that the 2-hydroxycyclohexadienone derived from 2,4-dimethylphenol cannot be isolated because it dimerises almost spontaneously, and the spectral properties of the dimer (III), as reported by Adler *et al.*, closely resemble those of maytenone. Further, as with maytenone, periodate fails to react with the dimer (III), and the latter does not exhibit any normal ketonic properties.

However, the dimer (III) is more susceptible to catalytic hydrogenation than is maytenone, although the latter's stability may well be the consequence of steric factors.

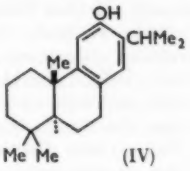
The pyrolytic decomposition of maytenone does not reverse the mode of formation and, as has been outlined above, it involves the elimination of propene from one of the units. Although the precise structure of maytenone has not yet been determined, many of the observed reactions can be interpreted on the assumption that the biogenesis of maytenone involves an oxidation of ferruginol (IV) to the corresponding hydroxycyclohexadienone (V) which then dimerises to a structure (VI) which we now use to illustrate the reactions of maytenone. Because the gas produced from the pyrolysis of maytenol is impure propene it is assumed that the propene is derived from the unit (B) containing the saturated carbonyl group. The C_{17} catechol has not been detected in the pyrolysis

[7] King, King, and Manning, *J.*, 1957, 563.
[8] Review: Wessely, *J. Roy. Inst. Chem.*, 1959, 424.
[9] Adler, Junghahn, Lindberg, Berggren, and Westin, *Acta. Chem. Scand.*, 1960, **14**, 1261.

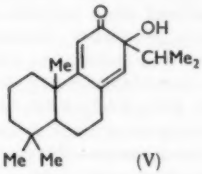
products from maytenol, which reaction may well proceed by a fundamentally different mechanism. In the case of the other unit (A) of maytenone which gives rise to the isopropylpodocarpanediol (hydroxytotarol) in the pyrolysis it would be necessary to



(III)

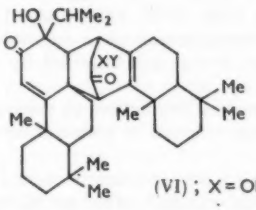


(IV)

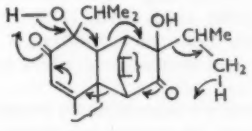


(V)

postulate a migration of the isopropyl grouping, on the basis of structure (VII). Such a rearrangement could well occur in the biogenesis of totarol which does not obey the isoprene rule.



(VI); X = OH, Y = $CHMe_2$



(VII)

The final formulation of maytenone may well depend on a possible synthesis by oxidation of ferruginol or totarol or a mixture of the two diterpenes. These experiments are now in progress in our laboratories.

Experimental

M. p.s are uncorrected. Ultraviolet absorption spectra were measured on ethanolic solutions and optical rotations were measured for the D line in chloroform except where otherwise stated.

Isolation of Maytenone.—The yellow outer root bark (1 kg.) of *Maytenus dispermus* was extracted by the method used in the isolation of pristimerin.[1] More maytenone was obtained by Soxhlet extraction of the " spent " bark with ether. The compound was finally crystallised from ether–light petroleum (b. p. 60—80°) as colourless needles (average 0·3 g. per batch), m. p. 197° (decomp.), $[\alpha]_D^{18}$ +115° (Found: C, 79·4; H, 9·85. Calc. for $C_{40}H_{60}O_4$: C, 79·4; H, 10·0%); $\lambda_{max.}$ 212 and 252 mμ (log ε 3·93 and 3·91); $\nu_{max.}$ (carbon tetrachloride solution) 858, 885, 911, 1025, 1046, 1120, 1140, 1157, 1175, 1240, 1275, 1310, 1370, 1390, 1430, 1460, 1600, 1680, 1710, 2920, 3478, and 3610 $cm.^{-1}$. A counter-current distribution of maytenone over 100 tubes in methanol–light petroleum (b. p. 60—80°) was followed by light-absorption measurements on the contents of each tube; the plot showed only a single peak.

Maytenol.—Maytenone (1 g.) was dissolved in dry ether (50 c.c.), and the solution added dropwise to a stirred suspension of lithium aluminium hydride (1 g.) in dry ether (50 c.c.). The mixture was stirred at room temperature for 10 hr. and then the excess of reagent was destroyed by addition of water (20 c.c.) followed by dilute hydrochloric acid. The product, *maytenol*, was extracted from the mixture with ether, and crystallised from aqueous ethanol as prisms (0·9 g.), m. p. 265—266° (decomp.), $[\alpha]_D^{20}$ +114° [Found, on a sample sublimed at 190°/5·5 × 10^{-4} mm.: C, 79·5; H, 10·4%; *M* (Rast), 574. $C_{40}H_{62}O_4$ requires C, 79·2; H, 10·3%; *M*, 607]; $\lambda_{max.}$ 204 and 255 mμ (log ε 3·89 and 3·78, respectively); $\nu_{max.}$ (potassium bromide disc) showed max. at 842, 857, 884, 1019, 1066, 1150, 1166, 1212, 1256, 1311, 1373, 1462, 1649, 1671, 2947, and 3442 $cm.^{-1}$; ν (in carbon tetrachloride solution) 3410, 3500, and 3610 $cm.^{-1}$ (OH). The corresponding *acetate* (acetic anhydride–pyridine) had m. p. 144—146° after crystallisation from aqueous ethanol (Found: C, 77·3; H, 10·0. $C_{42}H_{64}O_5$ requires C, 77·7; H, 9·95%).

Oxidation of maytenol with chromic acid, either in pyridine or glacial acetic acid solution, re-formed maytenone.

Dihydromaytenol.—Maytenone (1 g.) was dissolved in dry tetrahydrofuran (60 c.c.), lithium aluminium hydride (1 g.) was added, and the mixture was heated under reflux for 1½ hr. and then cooled. The excess of reagent was destroyed by the successive addition of water and dilute hydrochloric acid and the product, *dihydromaytenol*, was isolated by ether extraction and crystallised from aqueous methanol; it then formed prisms (0·4 g.), m. p. 239—240° (decomp.), $[\alpha]_D^{20}$ +41·0° (Found: C, 78·6; H, 10·5. $C_{40}H_{64}O_4$ requires C, 78·9; H, 10·6%). No maxima were present in the ultraviolet absorption curve between 200 and 400 mμ; $\nu_{max.}$ (in carbon tetrachloride) 879, 1016, 1031, 1079, 1114, 1143, 1157, 1178, 1216, 1248, 1268, 1366, 1377, 1388, 1467, 1662, 1707, 2843, 2933, and 3406 cm.$^{-1}$.

The same product was obtained from the reduction of maytenol under similar conditions.

Anhydromaytenone.—Maytenone (0·2 g.) was dissolved in acetic anhydride (20 c.c.) containing perchloric acid (1 drop), and the solution was kept at room temperature for 1 hr. The mixture was then poured into cold water and kept overnight. Next day the precipitate, *anhydromaytenone*, was crystallised from aqueous ethanol, forming prisms (0·15 g.), m. p. 232—233° $[\alpha]_D^{20}$ +98° [Found: C, 81·6; H, 9·85%; *M* (Rast), 601. $C_{40}H_{58}O_3$ requires C, 81·85; H, 9·95%; *M*, 587]; $\lambda_{max.}$ 222 and 246 mμ (log ε 3·85 and 3·94); $\nu_{max.}$ (carbon tetrachloride) 893, 939, 968, 1020, 1050, 1095, 1120, 1140, 1155, 1165, 1190, 1270, 1325, 1335, 1370, 1390, 1455, 1625, 1680, 1725, and 2900 cm.$^{-1}$. Anhydromaytenone gave negative reactions with Schiff's reagent and ammoniacal silver nitrate and it was not oxidised by chromic acid in pyridine.

The same product was obtained from maytenone by the action of boiling formic acid or boiling acetic acid, or acetic anhydride containing a trace of concentrated sulphuric acid or toluene-*p*-sulphonic acid.

Dehydrogenation of Maytenone.—Maytenone (3 g.) was intimately mixed with powdered selenium (7 g.) and heated under a long air condenser at 280—320° for 22 hr. The product was cooled and thoroughly triturated with ether in a mortar. The ethereal extract was clarified (charcoal) and the brown gum obtained after evaporation of the solvent was distilled at 0·6 mm.; a yellow resin (1 g.) was collected at 160—220°. This was dissolved in ether and then extracted with 5% aqueous sodium hydroxide in order to remove the phenols. This extract was acidified (dilute hydrochloric acid) and again extracted with ether, and the ethereal extract washed and dried. Removal of the solvent gave a yellow gum which, when treated with hot light petroleum (b. p. 60—80°) and cooled, yielded a slightly coloured crystalline product, m. p. 187—188°, which did not depress the m. p. of authentic 8-methyl-2-phenanthrol; $\lambda_{max.}$ 234, 260, 291, 326, 341, and 358 mμ (log ε 4·29, 4·77, 4·27, 3·91, 3·09, and 3·10, respectively). The corresponding acetate and methyl ether had m. p.s 134—135° and 133—134°, respectively, and did not depress the m. p.s of the corresponding authentic compounds.[11] The *s*-trinitrobenzene derivative had m. p. 186—187°, and distillation of the phenol with zinc gave 1-methylphenanthrene, m. p. 123° (lit.,[12] 123°).

Pyrolysis of Maytenone.—(i) 8-*Isopropylpodocarpane*-6,7-*diol* (*hydroxytotarol*). Maytenone (1 g.) was heated to 195—200° whereupon it rapidly decomposed with the evolution of a gas to give a yellow resin (0·903 g.). This product soon darkened in air and rapidly decomposed in alkaline solution to give a dark brown intractable gum. The product was purified by vacuum distillation [it distilled at 180—190° (bath temp.)/10^{-2} mm.] and chromatography on alumina, but it still failed to crystallise. Light absorption: $\lambda_{max.}$ at 203 and 287 mμ (log ε, 4·28 and 3·56). The corresponding *dibenzoate* (modified Schotten–Baumann method by dissolving the catechol in benzoyl chloride and adding alkali with shaking) formed plates (0·82 g.), m. p. 227—228° (from ethanol) not depressed on admixture with an authentic specimen (following paper) (Found: C, 79·7; H, 7·4. $C_{34}H_{38}O_4$ requires C, 80·0; H, 7·5%); $\lambda_{max.}$ 231 mμ (log ε 4·52), with an inflection at 275 mμ (log ε 4·48). Hydrogenolysis (lithium aluminium hydride) of the dibenzoate gave the free catechol as a brown gum which was distilled from a bulb tube to yield 8-*isopropylpodocarpane*-6,7-*diol* (6-*hydroxytotarol*) as a yellow resin, b. p. (bath temp.) 190°/10^{-2} mm. (Found: C, 79·2; H, 9·9. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·0%); $\lambda_{max.}$ 282 mμ (log ε 3·54). The *di*-p-*nitrobenzoate* (*p*-nitrobenzoyl chloride and pyridine at 100°) formed pale yellow prisms (methanol–chloroform), m. p. 210—212° (Found: C, 67·7; H, 6·0. $C_{34}H_{36}N_2O_8$ requires C, 68·0; H, 6·0%).

[10] Conradi and McLaren, *J. Amer. Chem. Soc.*, 1960, **82**, 4745.
[11] Short and Wiles, *J.*, 1936, 319.
[12] Pschorr, *Ber.*, 1906, **39**, 3106.

In water-saturated n-butanol, the purified isopropylpodocarpanediol had R_F 0·95 in an ascending chromatograph but only 0·83 on paper impregnated with 0·1N-aqueous sodium borate. Dehydrogenation of the purified isopropylpodocarpanediol with selenium by the method given for maytenone gave 8-methyl-2-phenanthrol, m. p. and mixed m. p. 181—183° (above).

(ii) *The* C_{17} *catechol* (II; R = OH, R′ = H). The mother liquors from the preparation of the isopropylpodocarpanediol dibenzoate (above) were evaporated, and the dried residue dissolved in ether. Lithium aluminium hydride (slight excess) was added and the solution heated under reflux for 1 hr. The reaction mixture was decomposed and, after extraction and removal of the solvent, the residue was distilled (bulb tube) to remove benzyl alcohol and then the higher boiling fraction was collected. It was dissolved in pyridine, treated with *p*-nitrobenzoyl chloride, and heated at 100° for 1 hr. The *di*-p-*nitrobenzoate* formed needles (methanol–chloroform), m. p. 186—188° (Found: C, 66·4; H, 5·6. $C_{31}H_{30}N_2O_8$ requires C, 66·65; H, 5·4%).

(iii) *Propene.* Pure dry maytenone (74 mg.) was placed in a tube connected to an evacuated gas cell, and the maytenone heated until decomposition was initiated. The evolved gas filled the cell at a calculated pressure of 20 mm.; the infrared spectrum of the gas showed the following maxima: 915, 995, 1036, 1447, 1478, 1642, 1667, 1818, 1840, 2951, 2977, 3076, and 3100 cm.$^{-1}$. This pattern is identical with that of authentic propene.

In another series of experiments, dry maytenone (26·5 mg.) was contained in a small tube connected to a vapour-phase chromatogram, oxygen-free nitrogen being used as the carrier gas in a 14-ft. column packed with Celite and a saturated solution of silver nitrate in ethylene glycol (20% by wt. of Celite). The gas evolved on pyrolysis of the maytenone was shown to be pure propene (78% for 1 mole per mole of maytenone), uncontaminated with water, ethylene, or paraffins.

Pyrolysis of maytenol at 270° in the same apparatus was shown to yield a mixture of gases including hydrogen, propane, ethylene, and water as well as propene.

Action of Formic Acid on Maytenol.—Maytenol (0·2 g.) was dissolved in formic acid (98%; 12 c.c.), and the solution heated under reflux for 1 hr. The mixture was cooled and poured into water, whereupon a precipitate was obtained which could not be crystallised but gave a green ferric test. Benzoylation (Schotten–Baumann) of this material gave a benzoate which crystallised from ethanol as plates, m. p. 224—225°, not depressed on admixture with 8-isopropylpodocarpane-6,7-diol dibenzoate (above).

We acknowledge the award of a Maintenance Grant from Monsanto Chemicals Limited (to R. J. M.) and we thank Dr. J. R. Price, of C.S.I.R.O., Melbourne, Australia, for a generous supply of *Maytenus dispermus* bark. We are also grateful to Professor D. H. R. Barton, F.R.S., for stimulating discussions on the chemistry of maytenone.

THE UNIVERSITY, NOTTINGHAM. [*Received, February 20th,* 1961.]

---

871. *The Synthesis of* 8-*Isopropylpodocarpane*-6,7-*diol* (6-*Hydroxytotarol*) *and of* 7,8-*Dimethoxypodocarpane.*

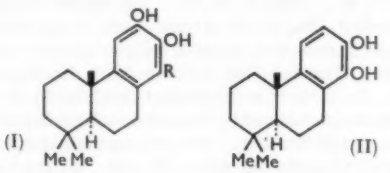
By N. F. ELMORE and T. J. KING.

Maytenone, $C_{40}H_{60}O_4$ (previous paper), decomposes on melting to give *inter al.* two phenolic materials. The synthesis of 8-isopropylpodocarpane-6,7-diol (6-hydroxytotarol) (I; R = $CHMe_2$) and of 7,8-dimethoxypodocarpane has shown that one of the phenols is 8-isopropylpodocarpane-6,7-diol and that the other is not identical, although it is isomeric, with podocarpane-7,8-diol (II).

THE bisditerpene maytenone [1] characteristically decomposes on melting at *ca.* 195° to give propene and a mixture which consists substantially of two catechols both of which appear to be related to diterpenes. One of these was readily purified as the sparingly

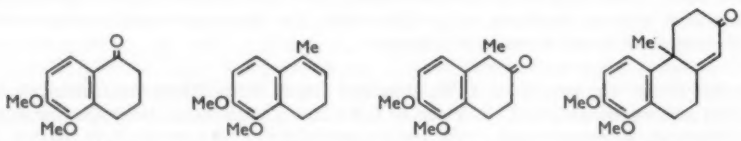
[1] Johnson, King, and Martin, preceding paper.

soluble dibenzoate and the other as the di-*p*-nitrobenzoate. Analysis and other considerations suggested that the crystalline dibenzoate was a derivative of a C_{20} catechol and a possible structure was that of 8-isopropylpodocarpane-6,7-diol (I; R = $CHMe_2$).



A quantity of totarol was available to us from the collection of the late Dr. W. F. Short through the kindness of Mrs. Short, and the 6-hydroxy-group was introduced into the molecule through 6-nitro- and 6-amino-totarol. The nitration was carried out following the method of Hodges and Raphael [2] for the nitration of 6-hydroxypodocarpane. The nitro-compound, characterised as its acetate, was readily reduced catalytically to aminototarol, previously prepared [3] by reduction of an azo-totarol. The aminophenol was diazotised in acetic acid solution and the resulting diazonium salt decomposed in boiling dilute sulphuric acid to give a moderate yield of a catechol which readily afforded a crystalline benzoate. A comparison of this benzoate with that derived from maytenone established their identity.

The second phenolic component of the pyrolysis of maytenone appears to be a C_{17} compound and the two most probable structures for this are 6,7- (I; R = H) and 7,8-dihydroxypodocarpane (II). We have synthesised the dimethyl ether of (II) by conventional means, following closely on Rao and Raman's synthesis of ferruginol.[4]

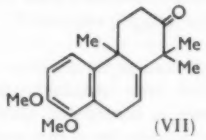


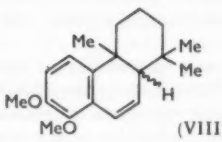
Methylation [5] of *o*-vanillin gave *o*-veratraldehyde which was treated with malonic acid and then reduced with sodium amalgam.[6] The β-(2,3-dimethoxyphenyl)propionic acid so obtained was homologated in excellent yield by the Arndt–Eistert method and the derived butyric acid or its methyl ester was cyclised with concentrated sulphuric acid to the tetralone (III) in 70% yield. Polyphosphoric acid as a cyclising agent gave consistently lower yields. The crystalline "styrene" (IV) was obtained in nearly quantitative yield by the action of methylmagnesium iodide in cold benzene on the ketone and was converted into the 2-tetralone (V) by reaction with lead tetra-acetate in acetic acid followed by acid isomerisation. Ring extension by the Robinson–Mannich procedure afforded the ketone (VI) in 37% yield, and this was then dimethylated, the derived ketone (VII) being purified through the semicarbazone.

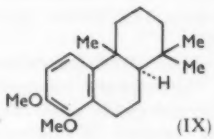
Huang-Minlon reduction of the pure semicarbazone removed the carbonyl oxygen and also caused migration of the double bond into conjugation with the benzene ring.

[2] Hodges and Raphael, *J.*, 1960, 50.
[3] Short and Wang, *J.*, 1951, 2979.
[4] Rao and Raman, *Tetrahedron*, 1958, **4**, 294.
[5] Cf. Barger and Silberschmidt, *J.*, 1928, 2924.
[6] Haworth, *J.*, 1927, 2282.

Although the product (VIII) was presumed to be a mixture of the *cis* and *trans* ring-fused compounds,[7] the final hydrogenation gave crystalline ether (IX). Subsequently the unsaturated ketone (VII) regenerated from the semicarbazone was reduced catalytically before removal of the carbonyl function but, as would be expected, reduction was much


(VII)


(VIII)


(IX)

slower than with (VIII). This product presumably had a *trans* ring fusion. Huang-Minlon reduction of the ketone afforded the same crystalline ether as obtained previously. A comparison of the infrared absorption spectra of this ether and of that derived from the pyrolysis product of maytenone established their non-identity, and moreover, a small amount of the derived catechol, prepared from the ether with hydriodic acid, failed to give a crystalline di-*p*-nitrobenzoate.

Experimental

All melting points were determined on a Kofler block.

6-*Nitrototarol.*—Cupric nitrate trihydrate (2·3 g.) was added to a solution of totarol (5 g.) in acetic anhydride (40 c.c.) with shaking, and the resulting green mixture was left overnight at room temperature. Water (200 c.c.) was added and when the acetic anhydride had reacted the solution was extracted with ether. The extract was washed (water, sodium hydrogen carbonate solution, water), dried, and evaporated to give a brown oil which was taken up in ethanol (50 c.c.). After this solution had been kept for several days in the refrigerator, 6-*nitrototarol* separated and crystallised from ethanol as long yellow needles (1·8 g.), m. p. 73—74·5° (Found: C, 72·7; H, 8·7; N, 4·6. $C_{20}H_{29}NO_3$ requires C, 72·45; H, 8·8; N, 4·25%). The *acetate* (acetic anhydride–sulphuric acid) crystallised from ethanol as plates, m. p. 134—135° (Found: C, 70·7; H, 8·0; N, 4·0. $C_{22}H_{31}NO_4$ requires C, 70·75; H, 8·35; N, 3·75%).

6-*Aminototarol.*—6-Nitrototarol (650 mg.) in methanol (20 c.c.) was hydrogenated over Adams catalyst at atmospheric temperature and pressure. The calculated amount of hydrogen was absorbed in 30 min. and reduction then stopped. The residue, after catalyst and solvent had been removed, crystallised from light petroleum (b. p. 60—80°) as plates, m. p. 165—166° (lit.,[3] 166—167°).

6-*Isopropylpodocarpane*-6,7-*diol* (6-*Hydroxytotarol*) *Dibenzoate.*—6-Aminototarol (1·2 g.) in glacial acetic acid (40 c.c.) containing sulphuric acid (10 c.c. of 10%) was treated at −5° with aqueous sodium nitrite (1 c.c. containing 350 mg. of nitrite). After 1 hr. at 0°, urea was added to decompose excess of nitrous acid, and the solution was added gradually to refluxing sulphuric acid (20%; 90 c.c.) containing sodium sulphate (3 g.). When addition was complete the solution was cooled, diluted, and extracted with ether. The residue after evaporation of the ether, distilled at 160—180° (bath)/0·1 mm. to give a red resin having a green ferric reaction. The distillate (150 mg.) was dissolved in benzoyl chloride (1 c.c.) and shaken with aqueous sodium hydroxide during 5 min. The resulting *benzoate* was collected and crystallised from chloroform–ethanol, forming plates, m. p. 226—228° undepressed on mixture with a sample derived from maytenone (Found: C, 79·8; H, 7·1. $C_{34}H_{38}O_4$ requires C, 80·0; H, 7·5%). The infrared absorption curves of the two benzoate samples were identical.

γ-(2,3-*Dimethoxyphenyl*)*butyric Acid.*—β-(2,3-Dimethoxyphenyl)propionyl chloride (b. p. 106—107°/2 mm.; 47·5 g.), prepared from the acid [6] (52 g.) with thionyl chloride, in dry ether (200 c.c.) at 0°, was added slowly with stirring to a cold solution of diazomethane (from 90 g. of methylnitrosourea) in dry ether (1 l.). Evolution of nitrogen stopped after 1 hr., and after

[7] Wenkert and Stevens, *J. Amer. Chem. Soc.*, 1956, **78**, 2318, 5627.

a further 30 min. at room temperature the solvent was removed (vacuum) to afford the diazoketone as an orange-yellow viscous oil. This was dissolved in dry methanol (500 c.c.), and to the solution was added 2 c.c. of a 10% solution of silver benzoate in triethylamine.[8] The evolution of nitrogen was brisk and was maintained at a steady rate by further addition of the catalyst until it stopped abruptly. The solution was then boiled for 30 min., filtered and evaporated. The residue was distilled to give *methyl γ-(2,3-dimethoxyphenyl)butyrate* (42·7 g., 72·5%), b. p. 112°/2 mm., n_D^{12} 1·5080 (Found: C, 65·5; H, 7·65. $C_{13}H_{18}O_4$ requires C, 65·55; H, 7·6%).

When the Wolff rearrangement was carried out in aqueous dioxan with a silver oxide–sodium thiosulphate catalyst,[9] *γ-(2,3-dimethoxyphenyl)butyric acid* was obtained directly. However, the yields were variable and the method described above is considered preferable. The acid obtained in this way or by hydrolysis of the ester crystallised from benzene–light petroleum (b. p. 60—80°) as needles, m. p. 58·5—60° (Found: C, 63·9; H, 6·95. $C_{12}H_{16}O_4$ requires C, 64·25; H, 7·2%).

5,6-Dimethoxy-1-tetralone (III).—The above methyl ester (5 g.) was heated at 85—90° for 15 min. with sulphuric acid (85%; 50 c.c.). The resulting dark red solution was poured on ice and the precipitate was collected and crystallised from cyclohexane (charcoal) to give the *tetralone* in 70—75% yield as plates, m. p. 104—105°, $\lambda_{max.}$ 232 (log ε 4·26) and 281 mμ (log ε 4·12) (Found: C, 69·8; H, 6·5. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·85%). The *2,4-dinitrophenylhydrazone* crystallised from chloroform–methanol as deep red plates, m. p. 255—257°, $\lambda_{max.}$ 304 (log ε 4·01) and 401 mμ (log ε 4·43) (Found: C, 55·7; H, 4·9; N, 14·3. $C_{18}H_{18}N_4O_6$ requires C, 55·95; H, 4·7; N, 14·5%).

Similar yields of ketone were obtained by cyclising the acid under the same conditions.

3,4-Dihydro-5,6-dimethoxy-1-methylnaphthalene (IV).—The above tetralone (24 g.) in dry benzene (100 c.c.) was added during 1 hr. to a solution of methylmagnesium iodide (from 8·2 g. of magnesium) in benzene (200 c.c.) with stirring and cooling in ice. After 2 hr. at 0° a test sample gave no precipitate with cold methanolic dinitrophenylhydrazine sulphate. Next day the mixture was decomposed with ice-cold dilute sulphuric acid, and the benzene layer was separated, washed with aqueous sodium hydroxide, and evaporated. Methanol (40 c.c.) was added to the residue and after cooling overnight in the refrigerator the crystalline precipitate (21·2 g.) was collected. The *3,4-dihydro-5,6-dimethoxy-1-methylnaphthalene* crystallised from methanol in plates, m. p. 69—70°, $\lambda_{max.}$ 216 (log ε 4·27) and 268 mμ (log ε 4·10) (Found: C, 76·1; H, 7·8. $C_{13}H_{16}O_2$ requires C, 76·45; H, 7·9%).

5,6-Dimethoxy-1-methyl-2-tetralone (V).—Lead tetra-acetate (9·4 g.) was added gradually to an ice-cold solution of the above dihydronaphthalene (4·0 g.) in glacial acetic acid (50 c.c.), and the solution was allowed to warm to room temperature. After 45 min. the solution was poured into water and extracted with ether. The extract was washed and evaporated and the residue was boiled for 2 hr. with ethanol containing sulphuric acid (18%; 15 c.c.). The red solution so obtained was diluted with water (200 c.c.) and its ether extract was dried and distilled. The *2-tetralone* (2·7 g., 70%) came over at 115—116°/0·2 mm. as a yellow oil which solidified after several weeks (Found: C, 70·6; H, 6·75. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). The *2,4-dinitrophenylhydrazone* was obtained as yellow needles (from chloroform–methanol), m. p. 190—192°, $\lambda_{max.}$ 234 (log ε 4·29) and 366 mμ (log ε 4·35) (Found: C, 56·8; H, 5·0; N, 13·9; OMe, 14·7. $C_{19}H_{20}N_4O_6$ requires C, 57·0; H, 5·05; N, 14·0; 2OMe, 15·5%).

2,3,4,4a,9,10-Hexahydro-7,8-dimethoxy-4a-methyl-2-oxophenanthrene (VI).—A solution of potassium ethoxide (from 2·15 g. of potassium and 60 c.c. of ethanol) was added at 0° with swirling to a mixture of the 2-tetralone (8 g.) and diethylaminobutan-2-one methiodide (from 5·2 g. of ketone and 5·2 g. of methyl iodide) in dry benzene (60 c.c.) under nitrogen. The mixture was stirred during 15 min. and left at 0° for 1½ hr. The pale yellow solution was then boiled for 30 min., cooled, and decomposed with dilute sulphuric acid. The organic layer was separated and the aqueous layer extracted with ether. The combined organic solutions were washed, dried, and evaporated and the residue was distilled to give a resin, b. p. 140—160°/0·05 mm., which crystallised from cold ether (solid carbon dioxide) to give *2,3,4,4a,9,10-hexahydro-7,8-dimethoxy-4a-methyl-2-oxophenanthrene* (3·65 g., 36·9%). The analytical sample crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 107—108·5°, $\lambda_{max.}$ 233 mμ (log ε 4·38),

[8] Newman and Beal, *J. Amer. Chem. Soc.*, 1950, **72**, 5163.
[9] Bachmann and Struve, "Organic Reactions," Volume I, John Wiley and Sons, New York, 1942, p. 38.

$\nu_{max.}$ (in carbon tetrachloride) 1681 cm.$^{-1}$ (Found: C, 74·7; H, 7·3. $C_{17}H_{20}O_3$ requires C, 74·95; H, 7·4%). The *semicarbazone* formed needles (from ethanol), m. p. 198—199°, $\lambda_{max.}$ 228 (log ε 4·15) and 270 mμ (log ε 4·52) (Found: C, 65·4; H, 6·95. $C_{18}H_{23}N_3O_3$ requires C, 65·65; H, 7·05%).

1,2,3,4,4a,9-*Hexahydro*-7,8-*dimethoxy*-1,1,4a-*trimethyl*-2-*oxophenanthrene* (VII).—The above ketone (3·65 g.) was added at 30° under nitrogen to a solution of potassium (1·9 g.) in t-butyl alcohol (50 c.c.). The red solution was then cooled in ice, and methyl iodide (5 c.c.) was added in one portion. The contents of the flask were left at room temperature for 2 hr., and then boiled for 30 min. The oil obtained after dilution with water was collected in ether and isolated by evaporation as a gum whose infrared spectrum showed that it contained about 75% of a non-conjugated ketone. The crude ketone was converted into the *semicarbazone* which after crystallisation from ethanol had m. p. 208·5—211°, $\lambda_{max.}$ 226 mμ (log ε 4·26) (Found: N, 11·9. $C_{20}H_{27}N_3O_3$ requires N, 11·8%). The *hexahydrophenanthrone* was recovered by heating the semicarbazone with an acetic acid solution of pyruvic acid and sodium acetate and after isolation in the usual way distilled at 168—172° (bath)/0·15 mm. The distillate solidified in the receiver; its infrared absorption showed it to contain little if any αβ-unsaturated ketone, $\lambda_{max.}$ 274 mμ (log ε 3·20) (Found: C, 75·7; H, 8·25. $C_{19}H_{24}O_3$ requires C, 75·95; H, 8·05%).

1,2,3,4,4a,10a-*Hexahydro*-7,8-*dimethoxy*-1,1,4a-*trimethylphenanthrene* (VIII).—The above semicarbazone was heated in diethylene glycol (50 c.c.) containing hydrazine hydrate (100%; 3 c.c.) and potassium hydroxide (4 g.) at 150° for 1 hr. and then at 190° for 5 hr. The oil extracted by ether from the diluted and acidified solution gave a green ferric reaction and was methylated (acetone–methyl sulphate–potassium carbonate) to give the *product*, which distilled at 110—120° (bath)/0·01 mm.; this did not display hydroxyl group absorption in the infrared spectrum; $\lambda_{max.}$ 227 (log ε 4·37) and 268 mμ (log ε 3·91) (Found: C, 79·5; H, 9·25. $C_{19}H_{26}O_2$ requires C, 79·9; H, 9·15%).

trans-1,2,3,4,4a,9,10,10a-*Octahydro*-7,8-*dimethoxy*-1,1,4a-*trimethyl*-2-*oxophenanthrene*.—The above hexahydrophenanthrone (regenerated from the semicarbazone; 1·5 g.) was hydrogenated in acetic acid over 10% palladised charcoal, the theoretical uptake of hydrogen being achieved after 48 hr. The *product*, isolated in the usual manner, distilled at 190—195° (bath)/0·3 mm. and slowly crystallised (Found: C, 75·1; H, 8·5. $C_{19}H_{26}O_3$ requires C, 75·45; H, 8·65%).

trans-1,2,3,4,4a,9,10,10a-*Octahydro*-7,8-*dimethoxy*-1,1,4a-*trimethylphenanthrene* (IX).—(*a*) The above saturated ketone was reduced in the same way as described for its unsaturated derivative. Remethylation and distillation of the product afforded 6,7-*dimethoxypodocarpane* as an oil, b. p. 135—145° (bath)/0·01 mm., which crystallised as plates, m. p. 48—52° (Found: C, 79·4; H, 9·7. $C_{19}H_{28}O_2$ requires C, 79·1; H, 9·8%).

(*b*) 1,2,3,4,4a,10a-Hexahydro-7,8-dimethoxy-1,1,4a-trimethylphenanthrene (128 mg.) was hydrogenated in acetic acid at room temperature and pressure over 5% palladised charcoal. Hydrogen uptake was complete in 10 hr. The product (75 mg.), isolated in the usual way, had b. p. 180—184° (bath)/0·15 mm., and solidified as plates, m. p. 52—53° undepressed by the material prepared by route (*a*), $\lambda_{max.}$ 277 mμ (log ε 3·12) (Found: C, 79·5; H, 9·9%).

The infrared absorption curves of this material and the dimethyl ether prepared from the phenol derived from maytenone showed many points of dissimilarity.

Our thanks are due to Professor A. W. Johnson for his interest and encouragement and to the Department of Scientific and Industrial Research for a grant (to N. F. E.).

Department of Chemistry, University of Nottingham. [*Received, February 20th,* 1961.]

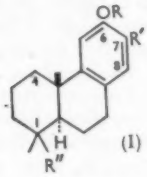
XUM

872. *The Synthesis of Podocarpane-6,7-diol, a Degradation Product of Maytenone.*

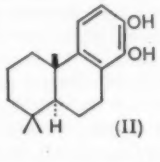
By J. A. Hill, A. W. Johnson, and T. J. King.

Podocarpane-6,7-diol has been synthesised from podocarpan-6-ol and shown to be identical with one of the phenolic pyrolysis products of maytenone.

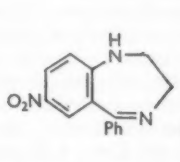
The bis-diterpene maytenone [1] has been shown to decompose, when heated, into propene, 8-isopropylpodocarpane-6,7-diol (6-hydroxytotarol [2]), and a phenol, $C_{17}H_{24}O_2$, the probable structure of which was podocarpane-6,7- (I; R = H, R′ = OH, R″ = Me) or -7,8-diol (II). The latter (II) was synthesised [2] in the racemic form and shown not to be identical with the degradation product. The former has now been prepared from podocarpic acid and is identical with the degradation product.



(I)



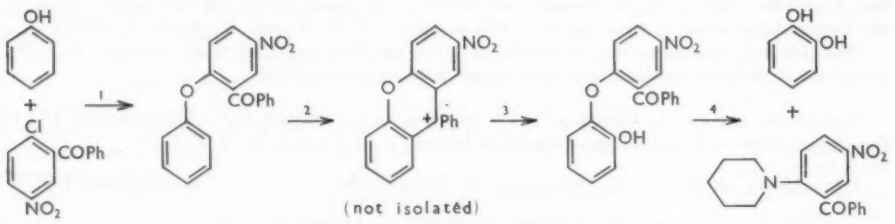
(II)



(III)

Initial attempts to synthesise (±)-podocarpane-6,7-diol by a method derived from Rao and Raman's route [3] to ferruginol and used for the preparation of the corresponding 7,8-dihydroxy-isomer [2] proved troublesome and were abandoned when a plentiful supply of podocarpic acid was made available to us through the courtesy of Dr. P. K. Grant of the Dominion Laboratory, Wellington. Podocarpic acid is readily converted into podocarpan-6-ol (I; R = R′ = H, R″ = Me) through the corresponding methoxy-alcohol and aldehyde,[4] and provides an obvious starting point for the synthesis.

Previous attempts to hydroxylate podocarpan-6-ol had been made by Martin [5] by conventional routes, namely, (*a*) oxidation by potassium nitrosodisulphonate, followed by reduction of the expected quinone, (*b*) oxidation of the 7-acetyl derivative with hydrogen peroxide, and (*c*) oxidation of the 7-acetate methyl ether with peracetic acid, but these were unsuccessful. We have also tried to introduce the second hydroxyl group *via*



Reagents: 1, KOH–EtOH; 2, H_2SO_4; 3, H_2O_2; 4, piperidine.

7-aminopodocarpan-6-ol,[4a] both by diazotisation (a method successful in the preparation of 6-hydroxytotarol [2]) and by oxidation to the *o*-quinone followed by reduction, but again without success. We finally turned to the method originated by Loudon and his

[1] Johnson, King, and Martin, *J.*, 1961, 4420.
[2] Elmore and King, *J.*, 1961, preceding paper.
[3] Rao and Raman, *Tetrahedron*, 1958, **4**, 294.
[4] (*a*) Hodges and Raphael, *J.*, 1960, 50; (*b*) Bible, jun., *Tetrahedron*, 1960, **11**, 22.
[5] Martin, unpublished work, University of Nottingham.

co-workers [6] for the specific *ortho*-hydroxylation of simple phenols and modified by Fishman, Tomasz, and Lehman [7] for use with more complex compounds. The essential features of the method are set out in the chart.

The possibility of carrying out these reactions with podocarpan-6-ol was first tested with the more readily available methyl podocarpate, which reacted with 2-chloro-5-nitrobenzophenone in alcoholic potassium hydroxide to give the crystalline ether (I; R = 2-benzoyl-4-nitrophenyl, R′ = H, R″ = CO_2Me) which was readily cyclised and oxidised to the hydroxy-ether (I; R = 2-benzoyl-4-nitrophenyl, R′ = OH, R″ = CO_2Me). The infrared absorption at 1666 cm.$^{-1}$ of the carbonyl group in the hydroxy-compound (1681 cm.$^{-1}$ before hydroxylation) indicated considerable hydrogen bonding and confirmed the presence of the hydroxyl group.

The model experiments having proved successful, similar transformations were easily carried out with podocarpan-6-ol. Difficulty was, however, experienced in isolating the dihydric phenol after the final reaction (fission of the ether with piperidine) because of the low solubility of the catechol in aqueous alkali and its ready aerial oxidation in that medium (5-nitro-2-piperidinobenzophenone is not soluble in acid), and the use of light petroleum and Claisen's alkali in the working-up was also unsatisfactory. However, when ethylenediamine was substituted for piperidine as the reagent, the fission was more complete (this was first tested with the nitrobenzophenone ether of α-naphthol) and the derived benzophenone was readily extracted from a benzene solution of the products with dilute acid, leaving the catechol. After one distillation this product, which was a gum giving an intense green ferric reaction, had an infrared spectrum virtually indistinguishable from that of the decomposition product from maytenone. The identity was confirmed (mixed m. p., infrared absorption) by the preparation of its crystalline di-*p*-nitrobenzoate.

Aminolysis of the ether derived from methyl podocarpate similarly afforded 7-hydroxypodocarpic acid (I; R = R′ = OH, R″ = CO_2H), hydrolysis of the ester occurring during the reaction.

The acidic extracts from the aminolysis mixtures presumably contained 2-2′-aminoethylamino-5-nitrobenzophenone as the hydrochloride. When this was basified, the product obtained was no longer readily soluble in acid and showed no infrared carbonyl absorption, having instead absorption at 1620 cm.$^{-1}$ suggesting the presence of an azomethine linkage. It appears that cyclisation had occurred and that the compound must be formulated as 2,3-dihydro-7-nitro-5-phenyl-1*H*-benzo[*f*][1,4]diazepine (III). Direct reaction of 2-chloro-5-nitrobenzophenone with ethylenediamine also produced this derivative.

Experimental

M. p.s were determined on a Kofler block; alumina was Spence's grade H; infrared measurements refer to solutions in carbon tetrachloride.

Methyl O-(2-*Benzoyl*-4-*nitrophenyl*)*podocarpate*.—A mixture of methyl podocarpate (10·4 g.), 2-chloro-5-nitrobenzophenone [8] (8·3 g.), and potassium hydroxide (1·94 g.) was heated under reflux in 95% ethanol (320 c.c.) for 48 hr. Most of the solvent was then evaporated and the cooled mixture was diluted with water, acidified with dilute hydrochloric acid, and extracted with ether. The extract was dried ($MgSO_4$) and evaporated and the residue was transferred to an alumina (300 g.) column from which benzene eluted the *ether* (11·65 g., 72%). Further elution with chloroform and then methanol afforded methyl podocarpate (3·0 g.). Crystallisation from chloroform–ethanol without chromatography gave the product (41%) which separated from chloroform–ethanol as prisms, m. p. 152—154° (Found: C, 72·8; H, 6·0. $C_{31}H_{31}NO_6$ requires C, 72·5; H, 6·1%).

Methyl O-(2-*Benzoyl*-4-*nitrophenyl*)-7-*hydroxypodocarpate*.—The above ether (1 g.) in acetic acid (24 c.c.) was treated dropwise with cooling and shaking with ice-cold concentrated sulphuric

[6] Loudon, Robertson, Watson, and Aiton, *J.*, 1950, 55; Loudon and Scott, *J.*, 1953, 265.
[7] Fishman, Tomasz, and Lehman, *J. Org. Chem.*, 1960, **25**, 585.

acid (32 c.c.). After 30 min., the deep red solution was diluted with acetic acid (40 c.c.), and 30% hydrogen peroxide (100 c.c.) was added slowly. After 30 min., the now colourless solution was poured into water and the precipitate (0·94 g.) was collected and crystallised from chloroform–methanol. The analytical sample formed pale yellow prisms, m. p. 180—181° (Found: C, 70·5; H, 5·9. $C_{31}H_{31}NO_7$ requires C, 70·3; H, 5·9%).

6-(2-*Benzoyl*-4-*nitrophenoxy*)*podocarpane*.—A mixture of podocarpan-6-ol [4] (2 g.), 2-chloro-5-nitrobenzophenone (1·85 g.), and potassium hydroxide (0·43 g.) was heated under reflux in 95% ethanol (70 c.c.) for 48 hr. Most of the solvent was then evaporated and after the addition of water and acidification of the residue, the product was collected with ether. The brown gum which remained when the ether was evaporated was purified by elution from alumina with benzene–light petroleum (b. p. 60—80°) (1 : 1) to give the *ether* (1·2 g., 36%), which crystallised from ether–hexane as prisms, m. p. 109—117°, unchanged by further crystallisation (Found: C, 77·2; H, 6·5; N, 2·8. $C_{30}H_{31}NO_4$ requires C, 76·7; H, 6·65; N, 3·0%), $\nu_{max.}$ (in CCl_4) 1681 cm.$^{-1}$.

Further elution with the same solvents yielded another substance as a gum (0·27 g.) which crystallised on addition of ether. After recrystallisation from ether–hexane it was obtained as faintly yellow prisms, m. p. 114—115°, and identified as 2-*ethoxy*-5-*nitrobenzophenone* (Found: C, 66·6; H, 5·0. $C_{15}H_{13}NO_4$ requires C, 66·4; H, 4·8%), $\lambda_{max.}$ 281 and 329 mμ (log ε 4·17 and 4·05). This compound was also formed by reaction of 2-chloro-5-nitrobenzophenone with alcoholic potassium hydroxide. Elution of the chromatogram with benzene gave unchanged podocarpan-6-ol (1·06 g.).

In another experiment the yield of the required podocarpane ether was *ca.* 80% and 2-ethoxy-5-nitrobenzophenone was not obtained.

6-(2-*Benzoyl*-4-*nitrophenoxy*)*podocarpan*-6-*ol*.—The preceding ether (1 g.) was oxidised as described above. The *hydroxy-ether* (0·83 g.) so obtained crystallised from methanol as pale yellow needles, m. p. 169—170° (Found: C, 74·5; H, 6·2. $C_{30}H_{31}NO_5$ requires C, 74·2; H, 6·4%), $\nu_{max.}$ (in CCl_4) 1662 cm.$^{-1}$.

Podocarpane-6,7-*diol*.—The above hydroxy-ether (0·4 g.) and 98% ethylenediamine (8 c.c.) were heated under reflux for 4 hr. The cooled solution was diluted, acidified with dilute hydrochloric acid, and extracted with ether. The extract was washed with dilute hydrochloric acid and water, and then by distillation afforded *podocarpane*-6,7-*diol* (0·185 g., 86%), b. p. 170—180° (bath)/0·1 mm., as a pale yellow glass (Found: C, 78·3; H, 8·9. $C_{17}H_{24}O_2$ requires C, 78·4; H, 9·3%), that gave a dark green ferric reaction and afforded (in pyridine) a *di*-p-*nitrobenzoate*, colourless needles (from chloroform–methanol), m. p. 188—190°, undepressed on admixture with the di-*p*-nitrobenzoate of the C_{17} catechol obtained on pyrolysis of maytenone (Found: C, 66·6; H, 5·6; N, 5·0. $C_{31}H_{30}N_2O_8$ requires C, 66·65; H, 5·4; N, 5·0%).

7-*Hydroxypodocarpic Acid*.—The corresponding nitrobenzophenone ether (above) (0·7 g.) was treated as in the previous experiment. The *acid* (0·32 g.) was isolated without distillation as a solid which crystallised from methanol as colourless needles, m. p. 237—239°, with a green ferric reaction (Found: C, 70·0; H, 7·8. $C_{17}H_{22}O_4$ requires C, 70·3; H, 7·6%). The benzoate was not obtained crystalline, but dimethyl sulphate in acetone in the presence of potassium carbonate yielded *methyl* 7-*methoxy*-O-*methylpodocarpate*, b. p. 160—170° (bath temp.)/0·1 mm. (from a bulb tube) (Found: C, 71·9; H, 8·3. $C_{20}H_{28}O_4$ requires C, 72·25; H, 8·5%).

1-(2-*Benzoyl*-4-*nitrophenoxy*)*naphthalene*.—α-Naphthol (1·75 g.) was treated with 2-chloro-5-nitrobenzophenone (2·75 g.) as described above for methyl podocarpate and, after chromatography on alumina and elution with benzene–light petroleum (7 : 3), the *product* (1 g.) was obtained as a yellow gum (Found: C, 74·7; H, 4·2. $C_{23}H_{15}NO_4$ requires C, 74·8; H, 4·1%), $\lambda_{max.}$ 220, 256, and 286 mμ (log ε 4·84, 4·25, and 4·16 respectively).

Treatment of this nitrobenzophenone ether with 98% ethylenediamine as described above caused scission and the formation of α-naphthol (60%), m. p. 91—93°, and after basification of the acidic fraction there was obtained a dark yellow solid which formed yellow needles, m. p. 206—211°, on crystallisation from chloroform–methanol. The latter proved to be 2,3-dihydro-7-nitro-5-phenyl-1*H*-benzo[*f*][1,4]diazepine, identical with the product synthesised in the following experiment.

2,3-*Dihydro*-7-*nitro*-5-*phenyl*-1H-*benzo*[f][1,4]*diazepine*.—2-Chloro-5-nitrobenzophenone (1 g.) was heated under reflux in 98% ethylenediamine for 4 hr. The cooled solution was diluted and made alkaline with aqueous sodium hydroxide. The *product* was collected into chloroform and purified by chromatography on alumina, from which it was eluted by chloroform. It

separated from chloroform–methanol as yellow needles, m. p. 210—211° (Found: C, 67·3; H, 4·9; N, 15·2. $C_{15}H_{13}N_3O_2$ requires C, 67·4; H, 4·9; N, 15·7%).

We thank the Department of Scientific and Industrial Research for the award of a maintenance grant (to J. A. H.).

Department of Chemistry, Nottingham University. [*Received, May 24th*, 1961.]

---

873. *Tritertiary Arsine Complexes of Nickel, Palladium, and Platinum.*

By G. A. Barclay, R. S. Nyholm, and R. V. Parish.

The preparation and properties of the tritertiary arsine tridentate ligand, di-(3-dimethylarsinylpropyl)methylarsine (triarsine), are described. The complexes formed by this ligand with nickel, palladium, and platinum salts have been investigated. The bivalent metal halides form complexes having the general formula, $M^{II}X_2$ triarsine (X = Cl, Br, or I). The nickel(II) compounds are non-electrolytes in nitrobenzene and hence involve a five-co-ordinated nickel atom, but the platinum(II) derivatives behave as 1 : 1 electrolytes in nitrobenzene. The latter are therefore formulated as (Pt triarsine X)$^+X^-$; the ionised halide ion can be replaced by the perchlorate ion. The palladium(II) complexes are intermediate in their conductivity behaviour but resemble more closely the platinum than the nickel compounds; for example, they give perchlorates. The tendency to form five-co-ordinated complexes, *viz.*, $Pt^{II} < Pd^{II} \ll Ni^{II}$, is correlated with the $(n-1)d^9 \longrightarrow (n-1)d^8\,np$ energy separation in the free atom. The chemistry of five-co-ordinate d^8-complexes as a class is discussed.

Each of these metals also gives salts of the type $[M^{II}(\text{triarsine})_2][ClO_4]_2$; these are bi-univalent electrolytes in nitrobenzene, and studies of the reactivity of the co-ordinated and unco-ordinated ligand towards methyl iodide support the conclusion that in all three cases the metal atom is six-co-ordinated.

The behaviour of the compounds towards halogens is discussed and some platinum(IV) derivatives of the type [Pt triarsine X_2]ClO_4 are reported.

In view of the variety of metals and the range of oxidation states which are stabilised by the ditertiary arsine *o*-phenylenebisdimethylarsine,[1,2] the behaviour of tri- and tetra-tertiary arsines is of considerable interest. Some years ago we synthesised the tritertiary arsine [3] (I), henceforth referred to as triarsine, and a tetra-tertiary arsine [4] (II). The

(I) $Me{\cdot}As(CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}AsMe_2)_2$ $As(CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}AsMe_2)_3$ (II)

co-ordinating ability of the triarsine towards certain metal salts was briefly reported;[3] in the present paper we give details of the synthesis of the tridentate compound and discuss the nature and the structure of the complexes formed by nickel, palladium, and platinum.

The tritertiary arsine is prepared by making use of simple Meyer [5] and Grignard reactions as shown in the scheme. Starting from trimethylene chlorohydrin (III) the dichloro-3-chloropropylarsine (V) was prepared by the method of Gough and King.[6] The later stages in the synthesis are straightforward. The triarsine was obtained as a colourless oil which was oxidised fairly rapidly in air, forming a colourless, hygroscopic solid.

[1] Chatt and Mann, *J.*, 1939, 610.
[2] See Nyholm and Sutton, *J.*, 1958, 560, and references quoted therein.
[3] Barclay and Nyholm, *Chem. and Ind.*, 1953, 378.
[4] Barclay, unpublished observations.
[5] See Raiziss and Gavron, "Organic Arsenical Compounds," Chem. Catalogue Co., New York, 1923.
[6] Gough and King, *J.*, 1928, 2432.

XUM

$M^{II}X_2$ triarsine *Complexes.*—When an alcoholic solution of nickel bromide or nickel iodide is treated with the triarsine, dark compounds NiX_2 triarsine are precipitated. The chloro-complex could not be obtained pure; this in not unusual; similar difficulty was experienced by Jensen [7] when preparing the $NiX_2,2Et_3As$ compounds. These complexes

$$\underset{\text{(III)}}{HO\cdot[CH_2]_3\cdot Cl} \xrightarrow{1} \underset{\text{(IV)}}{HO\cdot[CH_2]_3\cdot AsO_3H_2} \xrightarrow{2} \underset{\text{(V)}}{Cl\cdot[CH_2]_3\cdot AsCl_2} \xrightarrow{3} \underset{\text{(VI)}}{Cl\cdot[CH_2]_3\cdot AsMe_2} \xrightarrow{4} \text{(I)}$$

Reagents: 1, $NaAsO_2$. 2, SO_2 + HCl, then $SOCl_2$. 3, MeMgI. 4, Mg, then $MeAsI_2$.

are virtually non-electrolytes in nitrobenzene; the molecular weight of the iodide in freezing nitrobenzene solution is that expected for a monomeric non-electrolyte (see Experimental section).

At first sight these data suggest that the nickel atom is five-co-ordinate but evidence as to the number of arsenic atoms which are co-ordinated is necessary to settle this point.

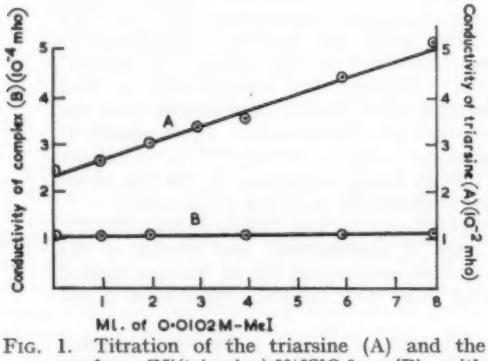


FIG. 1. Titration of the triarsine (A) and the complex $[Ni(triarsine)_2]^{2+}[ClO_4]^-_2$ (B) with methyl iodide.

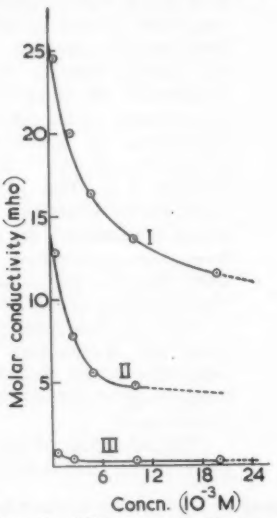


FIG. 2. Molar conductivity of (I) PtI_2 triarsine, (II) PdI_2 triarsine, and (III) NiI_2 triarsine.

This was established by titrating $[NiBr_2$ triarsine$]^0$ and the triarsine with methyl iodide. Whilst the triarsine shows a steady increase in conductivity consequent upon the reaction $R\cdot AsMe_2 + MeI \longrightarrow [R\cdot AsMe_3]^+I^-$, the complex does not (cf. Fig. 1). We conclude that no free $AsMe_2$ group occurs in the complex. It is, nevertheless, important to emphasise that even if conductivity did rise this would not necessarily show that the $AsMe_2$ group is free, for the Ni ← As bond could be quite reactive. In support of the view that all three arsenic atoms are co-ordinated, there is no evidence of oxidation of the nickel(II) complexes in air; a free $AsMe_2$ group might be expected to be oxidised readily in air. Also when the complex $NiBr_2$ triarsine is treated with bromine it is the nickel and not the $AsMe_2$ group that is oxidised. Finally, attempts to replace one of the halogen atoms by the perchlorate ion, as can be done with the palladium(II) and platinum(II) complexes, were unsuccessful; this suggests that neither halogen atom in the nickel complex is ionised.

The platinum complexes are much less intensely coloured than the nickel derivatives.

The former are soluble in certain polar solvents such as water and alcohol, but, unlike the nickel compounds, not in benzene or chloroform. This behaviour suggests that they are salts of the type [Pt triarsine X]$^+$X$^-$, which is confirmed by the molecular weight of the iodide in freezing nitrobenzene (see Experimental section) (it indicates virtually complete dissociation into two particles) and by the molar conductivity of the chloride, bromide, and iodide in nitrobenzene at 10^{-3}M-concentration (these are about 30 mho, the usual Λ_M value for a fully dissociated 1 : 1 electrolyte). Treatment of an alcoholic or aqueous solution of the PtX_2 triarsine complexes with perchloric acid yields compounds of the type [Pt triarsine X]ClO_4 which, as expected, are 1 : 1 electrolytes in nitrobenzene and nitromethane.

Palladium forms complexes of the type Pd^{II} triarsine X_2 and [Pd^{II} triarsine X]ClO_4 although solubility relations sometimes preclude the isolation of pure specimens (*e.g.*, the preparation of [Pd triarsine Br]ClO_4 from [Pd triarsine Br]Br is difficult. In good anion-solvating solvents such as water the Pd^{II} triarsine X_2 derivatives generally behave as 1 : 1 electrolytes but in nitromethane and nitrobenzene the molar conductivity of the iodide at 10^{-3}M-concentration suggests that about 50% of the molecules are dissociated into ions. This is supported by molecular-weight measurements for the iodide in freezing nitrobenzene: for a 0·325% solution (*i.e.*, $4{\cdot}4 \times 10^{-3}$M) the apparent molecular weight is 570, compared with a calculated value of 745 for the undissociated molecule. An effective method for comparing the nickel(II), palladium(II) and platinum(II) compounds is by measuring the molar conductivity at progressive dilutions in nitrobenzene. As may be seen from Fig. 2 the conductivity of the compound [Pd triarsine I]I is intermediate between those of the undissociated nickel complex and the largely ionised platinum compound.

The tendency for association of the type [M^{II} triarsine X]$^+$ + X$^-$ ⟶ [M^{II} triarsine X_2]^0 is thus in the order $Ni^{II} \gg Pd^{II} > Pt^{II}$. Similar behaviour with other ligands has been observed: the yellow $[Ni(CN)_4]^{2-}$ ion readily associates [8] with the CN^- ion to form the red 1 : 1 complex ion $[Ni(CN)_5]^{3-}$; however, the reaction between the corresponding $[Pd(CN)_4]^{2-}$ and $[Pt(CN)_4]^{2-}$ ions and the CN^- ion is negligible.[9] Similarly we have shown [10] that, for their capacity to associate with halide ions, the order is $[Ni(diarsine)_2]^{2+} > [Pd(diarsine)_2]^{2+} > [Pt(diarsine)_2]^{2+}$. The formation of a five-co-ordinate complex implies hybridisation of the $(n-1)d$, the ns, and the three np orbitals and this is most favoured if their energies are not too different. The energy separation between atomic orbitals increases with the *formal* charge on the metal atom and also with its effective nuclear charge.[11] Thus, the $ns \longrightarrow np$ separations for Zn^+ and Ga^{2+} are respectively 6·00 and 8·08 ev,[12] whilst the values for Cu^0, Ag^0, and Au^0 are 3·79, 3·65, and 4·63 ev. The effect of reducing the formal positive charge for d^8 complexes is illustrated by the following compounds: $[Cr(CO)_5]^{2-}$, $[Mn(CO)_5]^-$, $[Fe(CO)_5]$, and $[Co(PhCN)_5]^+$ (see refs. 13—15), whereas Ni^{2+} is four- or five-co-ordinate depending upon the ligand. An estimate of the ease with which the single p_z orbital can be hydridised with the four square $(n-1)d_{x^2-y^2}$ ns np_x np_y bonds is obtained from the energy required for the transition $(n-1)d^9 \longrightarrow (n-1)d^{8*}np$, where $d_8{}^*$ represents the spin-paired configuration, given in Table 1. The $(n-1)d \longrightarrow np$ separation increases with positive charge, and also from the first to the second to the third transition series provided that the charge on the metal ion is 1+ or less. It seems reasonable to assume that charge on the nickel(II), palladium(II), and platinum(II) atoms in the triarsine compounds lies between 0 and 1+ and that it is probably nearer

[7] Jensen, *Z. anorg. Chem.*, 1935, **229**, 265.
[8] McCullough, Jones, and Penneman, *J. Inorg. Nuclear Chem.*, 1960, **13**, 286.
[9] Reddy, Thesis, London, 1961.
[10] Harris, Nyholm, and Phillips, *J.*, 1960, 4379.
[11] Slater, "Quantum Theory of Atomic Structure," McGraw Hill, New York, 1960.
[12] Moore, "Atomic Energy Levels," U.S. Nat. Bur. Standards, Circular 467, 1952, Vol. II.
[13] Behrens and Kohler, *Z. Naturforsch.*, 1959, **14**b, 463; Behrens and Haag, *ibid.*, p. 600.
[14] Hieber and Wagner, *Z. Naturforsch.*, 1957, **12**b, 478.
[15] Malatesta, in "Progress in Inorganic Chemistry," Vol. I, ed. F. A. Cotton, Interscience Publ., Inc., New York, 1959; Malatesta and Sacco, *Z. anorg. Chem.*, 1953, **273**, 241.

Promotion energies (ev) for d^9 atoms and ions.[12]

Atom or ion	Co^0	Ni^+	Cu^{2+}	Rh^0	Pd^+	Ag^{2+}	Ir^0	Pt^+	Au^{3+}
$(n-1)d^9 \longrightarrow (n-1)d^{8*}np$ separation [a]	0·85	2·90	6·01	1·60	3·39	5·76	2·4	3·05	5·2

[a] *I.e.*, $d^9(^2D) \longrightarrow d^8(^1D)p(^2F)$.

the former;[16] if so, then the order of the $(n-1)d \longrightarrow np$ separation (1st row < 2nd row < 3rd row) agrees with the relative ease with which one can form the five-co-ordinate $[M^{II}$ triarsine $X_2]^0$ complexes. It is unlikely that the extra bond using the p_z orbital would be energetically equivalent to the other four bonds, and this should be reflected in the stereochemistry and bond lengths. We are indebted to Mr. H. M. Powell[17] and his colleagues for an *X*-ray crystal-structure study of $[Ni^{II}$ triarsine $Br_2]^0$, and this supports the above hypothesis. The structure (Fig. 3) shows that the Ni–Br bond normal to the square is notably longer (2·69 Å) than the other (2·37 Å). Some distortion of the bromine atom in the square occurs, probably owing to steric effects due to CH_2 groups, but the basic shape is that of a square pyramid with one long bond normal to the square. Crystal-structure data on the palladium(II) and platinum(II) compounds are incomplete but their structures are quite different, the complexes being essentially salts with the second bromine atom present as an ion.[18]

Whilst the chloro- and bromo-complexes of palladium(II) appear to exist only as salts of the type $[Pd$ triarsine $X]^+X^-$, the iodide (at least in nitrobenzene) exists in equilibrium with the non-ionic $[Pd$ triarsine $I_2]^0$ form, the tendency to form the non-ionic form

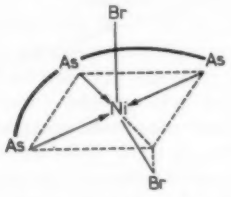


FIG. 3. Structure of $NiBr_2$ triarsine (AsAsAs = $Me_2As{\cdot}[CH_2]_3{\cdot}AsMe{\cdot}[CH_2]_3{\cdot}AsMe_2$).

increasing as the polarisability of the anion rises. An increase in polarisability is expected to decrease the charge on the metal atom to decrease the $(n-1)d \longrightarrow np$ separation, and hence to facilitate formation of the fifth bond. To sum up, the tendency to form five-co-ordinate d^8 complexes increases as: (i) the formal charge on the metal atom (oxidation state decreases), *i.e.*, $Ni^{II} < Co^I < Fe^0$; (ii) the effective nuclear charge on the metal atom decreases, *i.e.*, $Pt^{II} < Pd^{II} \ll Ni^{II}$; (iii) the polarisability of the anion increases, *i.e.*, $Cl^- < Br^- < I^-$. Earlier[10] we had noted that the relative ease with which nickel(II), palladium(II), and platinum(II) formed five-co-ordinate $[M^{II}$diarsine$_2$ $X]^+$ ions was in the *reverse* order to their Haissinsky electronegatives, *i.e.*, Ni (1·7) > Pd (2·0) > Pt (2·1). Electronegativities are related to ionisation potentials and these, in turn, are roughly proportional to promotion energies. Thus the approaches *via* electronegativity and promotion energies are not as different as they might appear. We now prefer the argument given in this paper to the simple charge picture because we consider it is probably more closely related to the actual situation obtaining around the metal atom. It is of interest to compare the structure of the five-co-ordinate NiX_2 triarsine complexes with that of other d^8 compounds. Infrared and dipole moment data[19] on $[Fe(CO)_3(RNC)_2]$ and the infrared spectrum[20] of the cation $[Co(CO)_3(Ph_3P)_2]^+$ indicate that these have a trigonal bipyramidal arrangement. This suggests that, as we pass from nickel(II) to

[16] Pauling, " The Nature of the Chemical Bond," Oxford Univ. Press, 1960, p. 399.
[17] Mair, Powell, and Henn, *Proc. Chem. Soc.*, 1961, 415.
[18] Powell, personal communication, 1961; see also *Proc. Chem. Soc.*, 1961, 170.
[19] Parish and Cotton, *J.*, 1960, 1440.
[20] Vohler, *Chem. Ber.*, 1958, **91**, 1235.

copper(I) to iron(0), not only does the tendency to form five-co-ordinate complexes increase, but also that the trigonal bipyramid tends to become the preferred structure. Thus it seems that as the formal positive charge on a metal ion decreases towards zero—or becomes negative—the stereochemistry is best discussed from a valence-bond or bond-pair repulsion picture; when the positive charge is appreciable, the converse is true.[21] More simply, the d^8 core in iron(0) is more easily polarised than in Ni^{2+}; if the five ligands around the Fe^0 atom then take up positions of maximum symmetry, a trigonal bipyramid will arise. However, in the Ni^{2+} ion the d^8 core is expected to be less easily polarised and hence to influence the position of ligands. To oversimplify, for a positively charged metal ion, on crystal-field theory, the more " rigid " non-bonding shell tends to decide where the ligands will go, whereas for a readily polarised ion the ligands tend to decide where the non-bonding electrons will be located. All of these arguments assume, of course, that steric effects are negligible. This is not always true, as has been demonstrated[17] in the case of the " planar " bromine atom in the $NiBr_2$ triarsine complex; further, the difference in energy between the square pyramid and the trigonal bipyramid arrangement is relatively small and steric effects alone might well, on occasions, cause a change from one shape to another. Thus, the square pyramidal shape of the five-co-ordinate cation $[PtI,QAS]^+$, where QAS is tris-(*o*-diphenylarsinophenyl)arsine, is attributed[18] to the steric requirements of the quadridentate group.

Bistriarsine Complexes.—Compounds having the general formula $[M^{II}(triarsine)_2][ClO_4]_2$ are conveniently prepared by treating the perchlorate of the metal with the triarsine in aqueous alcohol. However, one may also start from the monotriarsine derivative; addition of an excess of triarsine and perchloric acid effects conversion into the bistriarsine cation. In the case of nickel the bis-triarsine cation is produced when water is added to an acetone solution of $NiBr_2$ triarsine or the iodide. The almost black solution of the former becomes purple, owing to the reaction $2[Ni\ triarsine\ Br_2]^0 + water \longrightarrow [Ni(triarsine)_2]^{2+} + [Ni(H_2O)_6]^{2+} + 4Br^-(aq.)$. A study of the optical density of the solution confirms that half of the nickel is present as the bistriarsine cation. This behaviour is similar to that of $[Ni\ en_2Br_2]^0$ which is reported[22] to react with water to yield the trisethylenediamine cation and bromide ions. The corresponding palladium compound is red and the platinum complex is yellow. In all cases the molecular conductivity in nitrobenzene (~60 mho) and in nitromethane (~230 mho) at 10^{-3}M-concentration indicates that the complexes are bi-univalent electrolytes. The diamagnetism of the palladium and the platinum complex is not unexpected, but in the case of nickel the diamagnetism raises the question of the co-ordination number and in particular whether all three arsenic atoms are co-ordinated to the metal. As discussed above, titrations (Fig. 1) suggest very strongly that there is no free $AsMe_2$ group. Co-ordination of one or two $AsMe_2$ groups might reduce the reactivity of the third so much that it no longer reacts readily with methyl iodide, but this is most unlikely since the arsenic atoms are separated by three methylene groups and there is no reason to suppose that significant inductive effects would be felt through this chain. The supporting evidence—absence of oxidation of $AsMe_2$ groups (see above)—is confirmed by absorption spectra (Fig. 4). The cation $[Ni(triarsine)_2]^{2+}$ produces peaks at about the same wavelengths as does the complex ion $[Ni(diarsine)_3]^{2+}$ (*viz.*, 430 and 540 mμ),[23] but the intensities are different. The spectra of the five-co-ordinate iodo- and bromo-triarsinenickel(II) complexes are characterised by a very strong band (ε ~1500—2000) at about 400 mμ; this parallels the corresponding band near 490 mμ shown by the $[Ni(diarsine)_2Br]^+$ and $[Ni(diarsine)_2I]^+$ ions. In addition, however, the $Ni^{II}X_2$ triarsine complexes show further bands at longer wavelengths (~500—600 mμ), perhaps arising from the greater asymmetry of the triarsine complexes.

Believing that in $[M^{II}\ triarsine_2]^{2+}$ ions the metal is six-co-ordinate, we presume, for

[21] Nyholm, Tilden Lecture, *Proc. Chem. Soc.*, 1961, 273.
[22] Hieber and Levy, *Z. Electrochem.*, 1933, **39**, 26.
[23] Nyholm, *J.*, 1950, 2061.

reasons developed elsewhere,[24] that the metal atom is tetragonally co-ordinated as shown in Fig. 5, but until *X*-ray data are forthcoming this remains unproved.

Action of Oxidising Agents.—It was expected that halogens might react with the [M^{II} triarsine X_2] derivatives, producing complexes of the metal in higher oxidation states. As summarised recently,[10] the Ni^{II} diarsine complexes can be oxidised to both nickel(III) and nickel(IV) compounds, whereas palladium(II) and platinum(II) compounds give complexes of the quadrivalent metal. It was found that bromine and $NiBr_2$ triarsine in chloroform gave a black paramagnetic complex which was easily reduced back to the bivalent state. Attempts to prepare an analytically pure specimen of the compound $NiBr_3$ triarsine were not successful. The compound $PdBr_2$ triarsine with bromine in

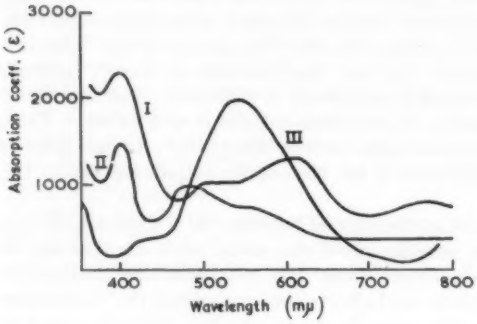


FIG. 4. Visible and ultraviolet absorption spectra of (I) NiI_2 triarsine, (II) $NiBr_2$ triarsine, and (III) $[Ni(triarsine)_2]^{2+}[ClO_4]^-_2$.

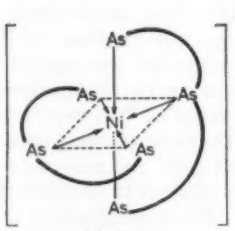


FIG. 5.

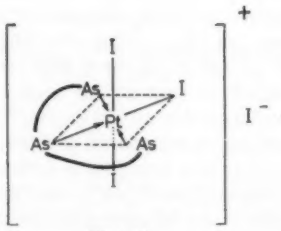


FIG. 6.

chloroform also gives a dark brown solution but it was not possible to isolate a pure palladium(IV) compound; the brown solution rapidly became clear, yielding the original yellow colour of the palladium(II) complex in solution. Presumably part of the arsine is oxidised by the palladium(IV) complex. With the platinum(II) compounds, however, oxidation takes place readily. Titration of [Pt triarsine Br]ClO_4 in chloroform (followed spectrophometrically) uses up two equivalents of bromine, and the orange platinic complex, [Pt triarsine Br_3]ClO_4, crystallises from the solution. This complex is a uni-univalent electrolyte in nitromethane, which confirms its formulation. The iodo-compound [Pt triarsine I]I with iodine in chloroform gives similarly a red, stable platinic complex Pt triarsine I_4. The molecular conductivity of this compound in nitromethane indicates that it is a uni-univalent electrolyte and hence is a typical octahedral platinum(IV) complex of the type [Pt triarsine I_3]I.* Since it is likely that the added iodine atoms take up *trans*-positions the structure is presumably that shown in Fig. 6.

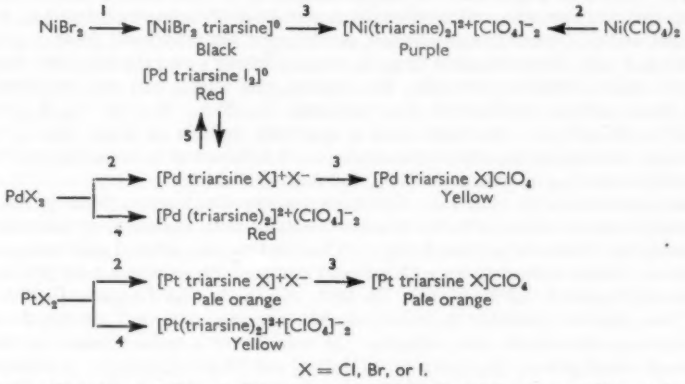
Isoelectronic octahedral complexes RhX_3 triarsine are also formed by tervalent rhodium; they will be described later.

* The possibility that this compound is the tri-iodide [Pt triarsine I]I_3 seems ruled out by the spectrum.

[24] Harris and Nyholm, *J.*, 1956, 4375; Harris, Nyholm, and Stephenson, *Nature*, 1956, **177**, 1127.

It is clear that although the triarsine stabilises certain higher oxidation states of the transition metals it is not as effective as the diarsine for this purpose.

The relations between the various compounds described above are shown in the annexed chart.



Reagents: 1, Triarsine in EtOH. 2, Triarsine in aq. EtOH. 3, $HClO_4$ in aq. EtOH. 4, Excess of triarsine + $HClO_4$ in aq. EtOH. 5, I^- where X = I.

Bivalent metal complexes.

Experimental

Dichloro-3-chloropropylarsine.—Trimethylene chlorohydrin (190 g.), by the method of Gough and King,[8] gave 100 g. of the dichloroarsine, b. p. 115—117°/12 mm.

3-Chloropropyldimethylarsine.—A Grignard reagent, from methyl iodide (142 g.), magnesium (24 g.), and sodium-dried ether (300 ml.), was filtered through glass wool and added slowly to a solution of dichloro-3-chloropropylarsine (100 g.) in dry ether (250 ml.), with stirring by a stream of dry nitrogen during the addition and in all subsequent operations. In a vigorous reaction a yellow solid separated, but this eventually disappeared, two layers being formed. After the addition the mixture was refluxed for 10 min. and decomposed with ammonium chloride solution. The ethereal layer was separated, and washed with water, saturated sodium hydrogen carbonate solution, and water. After drying ($MgSO_4$), the ether was removed in an atmosphere of nitrogen and the residue distilled, giving the *arsine* (65 g.), b. p. 60—62°/10 mm. (Found: C, 32·85; H, 6·4. $C_5H_{12}AsCl$ requires C, 32·9; H, 6·6%), as a colourless oil with a garlic odour.

Bis-(3-dimethylarsinylpropyl)methylarsine.—Reaction of magnesium (8 g.), 3-chloropropyldimethylarsine (64 g.), and dried ether (200 ml.) when initiated with methyl iodide, became vigorous. When reaction had subsided the mixture was refluxed for 15 min. and decanted from the excess of magnesium. Di-iodomethylarsine (56 g.), in the minimum quantity of benzene, was added slowly to the Grignard reagent. A vigorous reaction took place; the mixture was then refluxed for 20 min. and worked up as usual, giving the *triarsine* (32 g.), b. p. 180—182°/8 mm. (Found: C, 34·7; H, 6·9. $C_{11}H_{27}As_3$ requires C, 34·4; H, 7·1%), with a garlic-like unpleasant odour. As the triarsine darkened in air, forming a colourless solid, it was sealed in an inert atmosphere.

General.—All of the compounds described below are diamagnetic (all the results reported refer to 10^{-3}M-solutions at 25°). In nearly all cases they decompose near 250° without melting.

Dibromotriarsinenickel(II).—A warm solution of nickel bromide trihydrate (0·40 g.) in alcohol (5 ml.) was treated with the triarsine (0·57 g.) in alcohol (10 ml.). The resulting blue-black solution was heated under reflux for 10 min., then concentrated to about 5 ml. On cooling, the dark *complex* separated which recrystallised from alcohol as black plates (0·32 g.) (Found: C, 22·1; H, 4·5; Br, 26·6. $C_{11}H_{27}As_3Br_2Ni$ requires C, 21·9; H, 4·5; Br, 26·5%), soluble in common organic solvents such as chloroform and benzene, but insoluble in ether, virtually a non-electrolyte in nitrobenzene (Λ_M 1·3 mho).

Di-iodotriarsinenickel(II).—Nickel chloride hexahydrate (0·24 g.) and sodium iodide (0·40 g.) in water (3 ml.) were added to a solution of the triarsine (0·38 g.) in alcohol (10 ml.) and kept at 0° for several hours. The black *product* which separated recrystallised from acetone (0·45 g.) (Found: C, 18·9; H, 4·0%; *M*, cryoscopic in 0·42% nitrobenzene solution, 710. $C_{11}H_{27}As_3I_2Ni$ requires C, 18·9; H, 3·9%; *M*, 697). The compound, m. p. 275°, is soluble in acetone, chloroform, benzene, and nitrobenzene and is virtually a non-electrolyte in the latter (Λ_M 0·8 mho).

Bistriarsinenickel(II) *Diperchlorate*.—Nickel perchlorate heptahydrate (0·38 g.) in water (10 ml.) was treated with the triarsine (0·77 g.) in alcohol (20 ml.), and the resulting dark purple solution heated under reflux for 10 min. On cooling, the purple *salt* was deposited which recrystallised from acetone (yield 0·57 g.). (Found: C, 25·3; H, 5·3. $C_{22}H_{54}As_6Cl_2NiO_8$ requires C, 25·7; H, 5·3%). The compound is sparingly soluble in water and alcohol but soluble in acetone, nitrobenzene, and nitromethane. It behaves as a bi-univalent electrolyte in the last two solvents (Λ_M 52 mho in $PhNO_2$, 172 mho in $MeNO_2$).

Chlorotriarsinepalladium(II) *Chloride*.—Dichloroamminepalladium(II) (0·57 g.) in alcohol (30 ml.) was heated under reflux with the triarsine (0·40 g.) until evolution of ammonia ceased and all solid material dissolved (several hours). The solution was filtered and evaporated and the sticky residue washed several times with ice-cold acetone; on drying, a pale yellow powder (1·2 g.) remained (Found: C, 23·8; H, 5·0; Cl, 12·3. $C_{11}H_{27}As_3Cl_2Pd$ requires C, 23·5; H, 4·9; Cl, 12·6%). The *complex* is soluble in water, alcohol, nitrobenzene, and nitromethane but is insoluble in acetone, chloroform, and benzene. It behaves as a uni-univalent electrolyte in nitromethane and nitrobenzene (Λ_M 75·8 mho in $MeNO_2$ and 20·4 in $PhNO_2$). A potentiometric titration with silver nitrate in aqueous alcohol and a silver–silver chloride electrode showed that only one chlorine atom was ionised.

Chlorotriarsinepalladium(II) *Perchlorate*.—An aqueous-alcoholic solution of the compound [Pd triarsine Cl]Cl, prepared as above, was treated dropwise with 72% perchloric acid until no more precipitate was formed. The pale yellow *perchlorate*, obtained almost quantitatively, was washed with a little water and dried (Found: C, 21·3; H, 4·5. $C_{11}H_{27}As_3Cl_2O_4Pd$ requires C, 21·1; H, 4·4%). It is sparingly soluble in acetone, chloroform, and nitromethane and insoluble in water, alcohol, and nitrobenzene. It behaves as a uni-univalent electrolyte in nitromethane (Λ_M 77 mho).

Bromotriarsinepalladium(II) *Bromide*.—Dibromodiamminepalladium(II) (0·31 g.) was heated under reflux for several hours with the triarsine (0·38 g.) in alcohol (30 ml.). The resulting yellow solution was filtered, cooled, treated with ether, and left at 0° for several hours. The *compound* separated as yellow crystals (0·4 g.) (Found: C, 20·8; H, 4·6. $C_{11}H_{27}As_3Br_2Pd$ requires C, 20·3; H, 4·2%). It is readily soluble in acetone, nitrobenzene, and nitromethane but insoluble in benzene and chloroform. It behaves as a uni-univalent electrolyte in both nitromethane (Λ_M 79 mho) and nitrobenzene (Λ_M 18·0 mho).

Bromotriarsinepalladium(II) *Perchlorate*.—Prepared as was the corresponding chloro-perchlorate, the *compound* was obtained as a yellow crystalline powder (Found: C, 19·6; H, 4·1. $C_{11}H_{27}O_4As_3BrClPd$ requires C, 19·7; H, 4·1%). Solubilities are similar to those of the compound [Pd triarsine Cl]ClO_4. It behaves as a uni-univalent electrolyte in nitromethane (Λ_M 80 mho).

Iodotriarsinepalladium(II) *Iodide*.—Palladous hydroxide (0·14 g.), dissolved in a slight excess of dilute hydriodic acid, was treated with a solution of the triarsine (0·38 g.) in alcohol (10 ml.). The dark red solution was heated under reflux for a few minutes, filtered, and cooled; the *compound* (0·26 g.) separated as dark red needles which were washed with alcohol and dried (Found: C, 17·9; H, 3·8; I, 34·6%; *M*, cryoscopic in 0·325% solution in nitrobenzene, 570. $C_{11}H_{27}As_3I_2Pd$ requires C, 17·7; H, 3·7; I, 34·1%; *M*, 745). Solubilities are similar to, but less than, those of the compound [Pd triarsine Br]Br. The compound is partly ionised in both nitrobenzene and nitromethane (Λ_M 10·5 mho in $PhNO_2$ and 48 mho in $MeNO_2$).

Iodotriarsinepalladium(II) *Perchlorate*.—Considerable difficulty was encountered in preparing this derivative because it is more soluble than the iodo-iodide; it could not be obtained pure. The compound [Pd triarsine I]I (0·13 g.) in boiling alcohol (15 ml.) was treated with an excess of 72% perchloric acid (0·25 ml.). On cooling, orange-brown crystals (0·1 g.) separated and these were washed with alcohol and dried (Found: C, 19·6; H, 3·8. $C_{11}H_{27}As_3ClIO_4Pd$ requires C, 18·4; H, 3·8%). Solubilities are similar to those of the bromo-perchlorate. It is a uni-univalent electrolyte in nitromethane (Λ_M 83 mho).

Bistriarsinepalladium(II) *Diperchlorate*.—Palladium hydroxide (0·30 g.), suspended in 25%

perchloric acid (3 ml.), was treated with the triarsine (1·5 g.) in alcohol (10 ml.). The mixture was heated under reflux for 15 min., filtered, and cooled; the red *perchlorate* obtained recrystallised from aqueous acetone (Found: C, 24·7; H, 5·6. $C_{22}H_{54}As_6Cl_2O_8Pd$ requires C, 24·6; H, 5·1%). The complex is soluble in water, alcohol, acetone, nitrobenzene, and nitromethane and behaves as a bi-univalent electrolyte in the last of these (Λ_M 37·9 mho).

Chlorotriarsineplatinum(II) *Chloride*.—Sodium tetrachloroplatinate(II) tetrahydrate (0·45 g.) was shaken with the triarsine (0·38 g.) in absolute alcohol (20 ml.) until the liquid phase was colourless. The mixture was filtered, concentrated, diluted with ether, and cooled at 0°. White crystals of the *complex* (0·40 g.) separated (Found: C, 20·9; H, 4·7. $C_{11}H_{27}As_3Cl_2Pt$ requires C, 20·3; H, 4·2%). They were soluble in water, alcohol, and nitromethane, and sparingly soluble in nitrobenzene, but insoluble in acetone, chloroform and benzene. The product behaved as a uni-univalent electrolyte in nitromethane (Λ_M 68·2 mho).

Chlorotriarsineplatinum(II) *Perchlorate*.—Sodium tetrachloroplatinate(II) tetrahydrate (0·9 g.) in hot water (10 ml.) was added to the triarsine (0·70 g.) in hot alcohol (10 ml.), and the mixture was evaporated to dryness. The residue was extracted with hot alcohol (10 ml.) and the cooled, filtered solution treated dropwise with perchloric acid until precipitation was just complete. (An excess of perchloric acid causes the precipitate to redissolve.) The white *perchlorate* recrystallised from aqueous acetone (yield, 0·5 g.) (Found: C, 18·8; H, 4·2; Pt, 27·0. $C_{11}H_{27}As_3Cl_2O_4Pt$ requires C, 18·5; H, 3·8; Pt, 27·3%). It is soluble in acetone, nitrobenzene, and nitromethane, and sparingly soluble in hot alcohol, but insoluble in benzene and chloroform. It is a uni-univalent electrolyte in nitrobenzene (Λ_M 28·8 mho) and in nitromethane (Λ_M 87·7 mho).

Bromotriarsineplatinum(II) *Bromide*.—Tetrammineplatinum(II) dibromide (0·30 g.) in hot water (10 ml.) was refluxed with the triarsine (0·27 g.) in alcohol (10 ml.) for several hours (until evolution of ammonia ceased). The solution was evaporated to dryness at reduced pressure and the residue washed several times with ice-cold acetone, leaving pale yellow crystals (0·4 g.) of the *complex*; these recrystallised from chloroform–light petroleum (Found: C, 17·9; H, 3·9. $C_{11}H_{27}As_3Br_2Pt$ requires C, 17·6; H, 3·6%). The compound is soluble in water, alcohol, and nitromethane, and sparingly soluble in acetone and chloroform, but insoluble in benzene and nitrobenzene. It behaves as a uni-univalent electrolyte in nitromethane (Λ_M 68·2 mho).

Bromotriarsineplatinum(II) *Perchlorate*.—An aqueous solution of the compound [Pt triarsine Br]Br, prepared as above, was treated dropwise with perchloric acid and cooled to 0°. The white crystals of the *perchlorate* were filtered off and washed with ice-cold water (Found: C, 17·3; H, 3·6; Pt, 25·8. $C_{11}H_{27}As_3BrClO_4Pt$ requires C, 17·1; H, 3·6; Pt, 25·9%). The compound is soluble in acetone, chloroform, nitromethane, and nitrobenzene, but insoluble in water and alcohol. In nitrobenzene it behaves as a uni-univalent electrolyte (Λ_M 83·3 mho).

Iodotriarsineplatinum(II) *Iodide*.—This was prepared by treating an aqueous solution of the chloro-complex [PtCl triarsine]Cl with an excess of sodium iodide; the solution was evaporated until crystallisation began. The *compound* was obtained as large orange crystals, m. p. 252° (Found: C, 15·9; H, 3·3; Pt, 23·2%; *M*, cryoscopic in 0·57% nitrobenzene solution, 398. $C_{11}H_{27}As_3I_2Pt$ requires C, 15·8; H, 3·2; Pt, 23·4%; *M*, 833), soluble in acetone, chloroform, nitromethane and nitrobenzene, and sparingly soluble in warm alcohol, but insoluble in water. In both nitrobenzene (Λ_M 24 mho) and nitromethane (Λ_M 79 mho) it behaves as a uni-univalent electrolyte.

Bistriarsineplatinum(II) *Diperchlorate*.—Sodium tetrachloroplatinate(II) tetrahydrate (0·45 g.) in hot water (10 ml.) was added to the triarsine (0·77 g.) in alcohol (20 ml.). The yellow solution was warmed (5 min.), filtered hot, and treated with an excess of perchloric acid. On cooling, the required *perchlorate* (1·0 g.) was obtained as bright yellow crystals which recrystallised from aqueous alcohol (Found: C, 21·7; H, 5·0; Pt, 16·3. $C_{22}H_{54}As_3Cl_2O_8Pt$ requires C, 22·7; H, 4·7; Pt, 16·8%). The complex is soluble in acetone, nitrobenzene, and nitromethane but only sparingly soluble in water and alcohol. In both nitrobenzene (Λ_M 48 mho) and nitromethane (Λ_M 175 mho) it is a bi-univalent electrolyte.

Tribromotriarsineplatinum(IV) *Perchlorate*.—The compound [Pt triarsine Br]ClO_4 (0·5 g.) in chloroform (90 ml.) was treated with bromine (0·11 g.) in carbon tetrachloride (13 ml.). The platinic *complex* (0·6 g.) separated after a few minutes as orange leaflets; after some hours it was filtered off and washed with chloroform (Found: C, 14·9; H, 3·0; Pt, 21·2. $C_{11}H_{27}As_3Br_3ClO_4Pt$ requires C, 14·4; H, 2·9; Pt, 21·2%); it is less soluble than the platinous

derivatives but is slightly soluble in nitromethane and nitrobenzene in which it is a uni-univalent electrolyte.

Tri-iodotriarsineplatinum(IV) *Iodide*.—The complex [Pt triarsine I]I (0·5 g.) in chloroform (30 ml.) was treated with iodine (0·16 g.) in carbon tetrachloride (40 ml.). The solution was left for several hours at 0° and deposited a dark red powder. This *complex* recrystallised from acetone as red plates (0·6 g.) (Found: C, 12·2; H, 2·6; I, 47·5. $C_{11}H_{27}As_3I_4Pt$ requires C, 12·2; H, 2·5; I, 46·8%). As with the above Pt(IV) perchlorate, the compound is slightly soluble in nitromethane and in nitrobenzene in both of which it behaves as a uni-univalent electrolyte.

Analyses.—Platinum and palladium were determined by ignition of the compound after it had been moistened with concentrated sulphuric acid. Nickel was precipitated as the dimethylglyoxime complex after Kjeldahl decomposition of the compound.

SCHOOL OF CHEMISTRY, UNIVERSITY OF NEW SOUTH WALES,
KENSINGTON, N.S.W., AUSTRALIA.
WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER STREET,
LONDON, W.C.1.

[*Received, March 1st*, 1961.]

---

874. *High-temperature Studies of the System Calcium Oxide–Phosphorus Pentoxide.*

By J. H. WELCH and W. GUTT.

A revised phase diagram of the partial system $2CaO,P_2O_5$–CaO is presented, incorporating a new phase field for $\tilde{\alpha}$-$3CaO,P_2O_5$ and a region of solid solution between $3CaO,P_2O_5$ and $2CaO,P_2O_5$.

PORTIONS of the system CaO–P_2O_5 have been studied by several previous workers with differing conclusions.[1,2] Interest in the larger system CaO–P_2O_5–SiO_2 prompted us to reinvestigate the partial system $2CaO,P_2O_5$–CaO concerning which there is controversy in the literature. Furthermore, we have recently discovered a new form of tricalcium phosphate,[3,4] and revision of previous phase diagrams is thus needed.

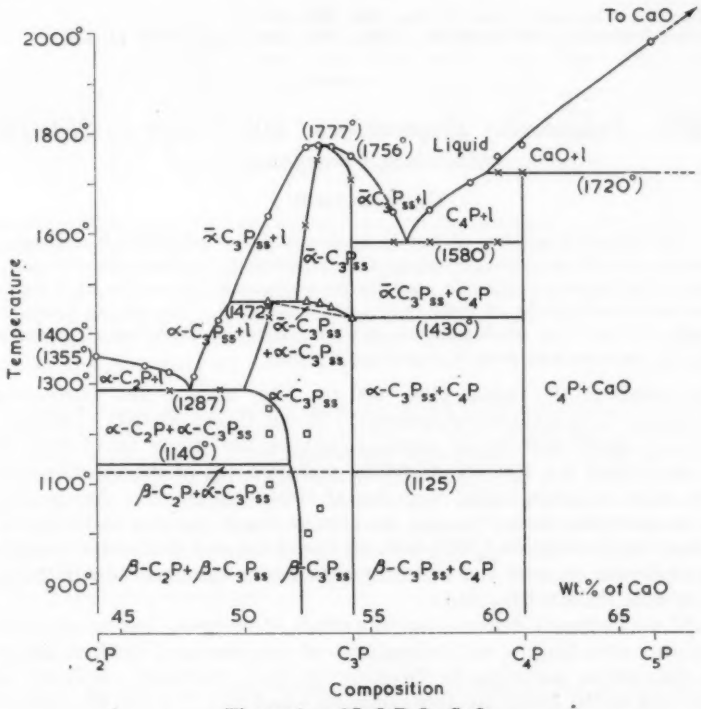
Experimental.—The preparation of materials and experimental procedure were as described earlier,[4] except for the following. Volatilization of phosphorus pentoxide from substances varying in compositions between $2CaO,P_2O_5$ and $3CaO,P_2O_5$, and of calcium oxide from those between $3CaO,P_2O_5$ and $4CaO,P_2O_5$ precluded the use of high-temperature *X*-ray analysis which requires prolonged heating of the specimen. Much of the system was explored by high-temperature microscopy, which is sufficiently rapid to avoid this difficulty, but for phase identification in the subsolidus region the traditional quenching method followed by *X*-ray analysis in a Guinier-type focusing camera was also used. Selective "free lime" analysis [5] was used to investigate the possibility of solid solution between $4CaO,P_2O_5$ and CaO.

Results and Discussion.—The new phase diagram is presented in the Figure and affirms by direct observation the congruent melting of $2CaO,P_2O_5$ (1355° c) and the incongruent melting of $4CaO,P_2O_5$ (1720°). In disagreement with earlier work [1] the liquidus curve reaches a maximum, not at $3CaO,P_2O_5$ (1756°), but very near the composition $53CaO,47P_2O_5$ (weight %) (1777°), and there is limited miscibility between $2CaO,P_2O_5$ and $3CaO,P_2O_5$. It has been established by 'free lime" analysis of compositions richer in lime than

[1] Trömel, *Stahl und Eisen*, 1932, **52**, 396; Trömel, *Mitt. Kaiser Wilhelm Inst. Eisenforsch.*, 1932, **14**, 25; Korber and Trömel, *Z. Elektrochem.*, 1932, **38**, 589; Korber and Trömel, *Arch. Eisenhüttenw.*, 1933, **1**, 7; Bredig, Franck, and Füldner, *Z. Elektrochem.*, 1932, **38**, 158; Bredig, Franck, and Füldner, *Z. Elektrochem.*, 1933, **39**, 959; Trömel, *Stahl und Eisen*, 1943, **63**, 21.
[2] Trömel, Harkort, and Hotop, *Z. anorg. Chem.*, 1948, **256**, 253.
[3] Nurse, Welch, and Gutt, *Nature*, 1958, **182**, 1230.
[4] Nurse, Welch, and Gutt, *J.*, 1959, 1077.
[5] Lerch and Bogue, *Ind. Eng. Chem., Analyt.*, 1930, **2**, 296.

$4CaO,P_2O_5$ that there is no solid solution between CaO and $4CaO,P_2O_5$; and no optical or *X*-ray evidence of solid solution between $4CaO,P_2O_5$ and $3CaO,P_2O_5$ was found.

High-temperature microscopy was successful in determining the course of the $\alpha \longrightarrow \bar{\alpha}$ inversion of $3CaO,P_2O_5$, the temperature of which rose with increasing solid solution of $2CaO,P_2O_5$. This technique did not reveal the $\alpha \longrightarrow \beta$ inversions of either $2CaO,P_2O_5$ or $3CaO,P_2O_5$, which were detected by quenching and *X*-ray analysis. Evidence that the quenching procedure was not wholly satisfactory was obtained from the observed presence



The system $2CaO,P_2O_5$–CaO.

○, Liquidus temperature. △, Temperature of $\alpha \longrightarrow \bar{\alpha}$ transition of C_3P_{ss} by optical examination. ×, Temperature of initial liquid formation. □ Points at which determinations were made with the focusing *X*-ray Guinier camera on quenched specimens. – – – – Broken lines indicate inferred boundary curves.

C = CaO, P = P_2O_5, l = liquid, ss = solid solution.

Temperatures are according to the International temperature scale of 1927.

of three phases, α-$2CaO,P_2O_5$, β-$3CaO,P_2O_5$, and α-$3CaO,P_2O_5$ in the composition $51CaO,49P_2O_5$ (weight %) after quenching from 1200° or 1250°. Presence of β-$3CaO,P_2O_5$ after quenching from a temperature above the inversion $\beta \longrightarrow \alpha$-$3CaO,P_2O_5$ which occurs at 1125° in pure $3CaO,P_2O_5$ (ref. 4) suggests the failure of quenching to preserve α-$3CaO,P_2O_5$. Although the $\alpha \longrightarrow \beta$-$3CaO,P_2O_5$ inversion in the pure compound takes place sufficiently slowly to be arrested easily by quenching, it appears that the presence of α-$2CaO,P_2O_5$ solid solution catalyses the inversion.

Precise location of the $\alpha \longrightarrow \beta$ inversions in $2CaO,P_2O_5$ and $3CaO,P_2O_5$ for mixtures lying between these compositions was not attempted, and the phase diagram shows boundaries projected at an assumed constant temperature from the inversion temperatures

determined for the pure compounds. For this purpose the $\alpha \longrightarrow \beta$ inversion of $3CaO,P_2O_5$ at 1125° was taken from our earlier work [4] and the $\alpha \longrightarrow \beta$ inversion of $2CaO,P_2O_5$ at 1140° is that reported by Hill, Faust, and Reynolds.[6] We have not investigated the low-temperature (−40° and +35°) inversions in $3CaO,P_2O_5$ noted by Koelmans, Engelsman, and Admiraal.[7]

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH, BUILDING RESEARCH STATION, WATFORD, HERTS. [*Received, March 10th*, 1961.]

[6] Hill, Faust, and Reynolds, *Amer. J. Sci.*, 1944, **242**, 458.
[7] Koelmans, Engelsman, and Admiraal, *J. Phys. and Chem. Solids*, 1959, **11**, 172.

---

875. *Deformation Frequencies of* OH *Groups in Nitrosylruthenium Complexes.*

By D. SCARGILL.

The infrared spectra of the hydroxo-complexes of nitrosylruthenium, namely, disodium hydroxotetranitronitrosylruthenate, hydroxotetra-ammine-nitrosylruthenium dichloride, and nitrosylruthenium hydroxide have been compared with those of their deuterated analogues. The strong band at 1000—970 cm.$^{-1}$ in the tetranitro- and tetra-ammine complexes arises from the deformation vibration of the hydroxyl group.

ABSORPTION bands in the region 1100—900 cm.$^{-1}$ for nitrato- and nitro-complexes of nitrosylruthenium have included assignments [1] to Ru–O and Ru–NO vibrations. Other work [2] has now shown that in the nitrato-complexes the strong broad band at 1000—940 cm.$^{-1}$ arises from the RuO–N stretching vibration (ν_2) of the co-ordinated nitrato-group.[3] In order to assign bands occurring at 1000—900 cm.$^{-1}$ in the spectra of some complexes of nitrosylruthenium having no nitrato-groups, spectra of the hydroxotetra-nitro-complex, $Na_2[RuOH(NO_2)_4NO]$, and its dihydrate and deuterated analogues have been compared with those of the hydroxotetra-ammine complex, $[RuOH(NH_3)_4NO]Cl_2$, and the hydroxide $RuNO(OH)_3,2H_2O$.

Studies [4,5] on hydroxyl deformation vibrations of inorganic hydroxides have shown that (i) both the stretching (ν) and deformation (δ) frequencies of the hydroxyl group are shifted on deuteration according to Hooke's law for a harmonic oscillator such that $\nu(OH)/\nu(OD)$ and $\delta(OH)/\delta(OD)$ are approximately equal to $\sqrt{2}$, (ii) $\delta(OH)$ tends to zero as the metal–oxygen distance increases (*i.e.*, the hydroxyl group becomes more ionic), and (iii) $\delta(OH)$ increases, and $\nu(OH)$ decreases, as the hydrogen bond becomes stronger.

RESULTS

Tetranitro-complex.—The spectrum of the dihydrate shows two superimposed bands in the region 3650—3450 cm.$^{-1}$, due to O–H stretching vibrations, when a sodium chloride prism is used in its measurement. When a lithium fluoride prism was used, the band at ~3550 cm.$^{-1}$ was resolved into two bands, assigned to the asymmetric and the symmetric stretching vibrations of the H_2O group (Table) and separated from the band at 3499 cm.$^{-1}$ arising from the stretching vibration of the hydroxyl group. A very weak band at 3764 cm.$^{-1}$ is attributed to a small proportion of free hydroxyl groups. On dehydration, the two bands at 3606 and 3545 cm.$^{-1}$, and the sharp band at 1620 cm.$^{-1}$, assigned to the HOH bending mode, disappear. Accompanying these changes, there is a shift in the bands from 3499 and 995 cm.$^{-1}$ in the

[1] Fletcher, *J. Inorg. Nuclear Chem.*, 1958, **8**, 277; Martin, Fletcher, Brown, and Gatehouse, *J.*, 1959, 76.
[2] Fletcher, Scargill, and Woodhead, unpublished work.
[3] Gatehouse, Livingstone, and Nyholm, *J.*, 1957, 4222.
[4] Hartert and Glemser, *Z. Electrochem.*, 1956, **60**, 746.
[5] Tarte, *Spectrochim. Acta*, 1958, **13**, 107.

spectrum of the dihydrate to 3518 and 923 cm.$^{-1}$ respectively in that of the anhydrous complex. The deuterated analogues show frequency shifts in all these bands with ratios ν(D)/ν(H) (Table) in accordance with those expected. The bands at 995 cm.$^{-1}$ for the dihydrate and at 923 cm.$^{-1}$ for the anhydrous complex can therefore be definitely assigned to the deformation vibration of the hydroxyl group.

Stretching and deformation frequencies (OH and OD) (in cm.$^{-1}$).

	$H_2O(D_2O)$ groups				OH(OD) groups					
	ν(OH)	δ(OH)	ν(OD)	δ(OD)	ν(OH)	δ(OH)	ν(OD)	δ(OD)	ν(OH)/ν(OD)	δ(OH)/δ(OD)
$Na_2[RuOH(NO_2)_4NO],2H_2O$	3606, 3545	1620	2688, 2644	1185	3499	995	2590	761	1·35	1·31
$Na_2[RuOH(NO_2)_4NO]$	—	—	—	—	3518	923	2595	[a]	1·35	~1·3
$[RuOH(NH_3)_4NO]Cl_2$	—	—	—	—	3455	971	2548	[a]	1·35	~1·3
$Ru(OH)_3NO,2H_2O$	—	1633	—	[b]	~3200	—	~2390	—	1·34	—

[a] Obscured by Nujol. [b] Obscured by contaminant.

Tetra-ammine Complex.—This has one medium and two strong bands in the 3 μ region. The first, at 3455 cm.$^{-1}$, is assigned to the hydroxyl stretching vibration and the last two, at 3243 and 3092 cm.$^{-1}$, to the N–H asymmetric and symmetric stretching vibrations respectively of the ammine ligands. Two bands occur in the region 1000—800 cm.$^{-1}$ and both are shifted on deuteration. However, the relation [6] between the rocking and the symmetric deformation frequencies of ammine ligands indicates that the band at 849 cm.$^{-1}$ is the ammine rocking frequency, so that the band at 971 cm.$^{-1}$ may be assigned to the hydroxyl deformation frequency.

Nitrosylruthenium Hydroxide.—The spectrum shows a strong broad band at 3200 and a weak band at 1633 cm.$^{-1}$, both shifted on deuteration and assignable to O–H stretching and H–O–H bending modes (Table). The spectra for preparations from nitric and sulphuric acid solutions show other weak bands in the regions 1500—1250 and 1150—900 cm.$^{-1}$ respectively, which are not shifted on deuteration. These bands, which are absent from the spectrum of the preparation from chloride solution, are assigned to nitrato- and sulphato-groups respectively. As there are no bands from 1200 to 670 cm.$^{-1}$ which can be assigned to deformation vibrations of the hydroxyl groups, it is concluded that these groups are here more ionic than in the other compounds studied.

Discussion

Comparison of the hydroxyl deformation (δ) and stretching (ν) frequencies in the anhydrous tetranitro-complex with those in the tetra-ammine complex gives −0·76 for the ratio $(\delta_I - \delta_{II})/(\nu_I - \nu_{II})$. As this approximates to the value of −0·66 found by Hartert and Glemser [4] and by Tarte [5] for hydroxyl groups with hydrogen bonds of intermediate strength, their empirical equation for the radius of the hydroxyl group with reference to the cation, $r(K)_{OH} = 8{\cdot}9 \times 10^{-4}\ (4720 - \delta - 0{\cdot}7\nu)$, may be used. This gives values of 1·19 and 1·18 Å for the nitro- and ammine complex respectively, and indicates that in them the metal–oxygen distances are similar.

The water molecules in the tetranitro-dihydrate are shown to be weakly hydrogen-bonded by the high stretching frequencies and their ease of removal. On dehydration, a greater shift is observed for the deformation than for the stretching frequency of the hydroxyl group, such that $\Delta\delta/\Delta\nu = -3{\cdot}8$. Minor changes on dehydration also occur in the nitrosyl frequency (from 1897 to 1905 cm.$^{-1}$) and the frequencies of the nitro-groups (from 1444 to 1441 cm.$^{-1}$ and from 1334 to 1340 cm.$^{-1}$ with a reduction from 8 to 3 cm.$^{-1}$ in the splitting of the band at about 830 cm.$^{-1}$). These shifts are accounted for if (i) the water molecules are hydrogen-bonded to the nitro-groups (forming a cross-linked network in the crystal lattice), (ii) the hydroxyl groups are intermolecularly hydrogen-bonded to

[6] Svatos, Sweeny, Mizushima, Curran, and Quagliano, *J. Amer. Chem. Soc.*, 1957, **79**, 3313.

the nitrosyl groups (RuO–H · · · ONRu), and (iii) the metal–oxygen bond length is shorter in the hydrated complex as a consequence of (i).

It has already been noted by Brown [7] that the nitrosyl frequency is relatively low when hydroxyl groups are present in nitrosylruthenium complexes: this can be attributed to hydrogen-bonding [cf. (ii) above].

Experimental

Determination of Spectra.—Infrared spectra in the region 2—15 μ were obtained at 22° with a Hilger H800 double-beam spectrophotometer equipped with a rock-salt prism. A lithium fluoride prism was used in the 3 μ region to obtain better resolution and frequency measurements. Samples were examined as mulls in Nujol and hexachlorobutadiene, with thin (1—2 mm.) silver chloride windows prepared by rolling plates of ~5 mm. thickness between chromium-plated glazing sheets. When freshly prepared, such windows had good transmission, but deterioration limited their usefulness to about two weeks. Deuterated samples were mulled and mounted in a dry-box. Wavelengths were calibrated by means of the 2·999 μ band of ammonia and the characteristic bands of polystyrene.

Preparations.—Disodium hydroxotetranitronitrosylruthenate. The procedure of Fletcher *et al.*[8] was modified to afford the dihydrate complex free from sodium chloride (formed as a major contaminant by the procedure described) by quickly washing the mixed crystals obtained with alcohol and extracting them with 20 ml. batches of acetone. The acetone was evaporated quickly at room temperature to minimise decomposition, and the residue dissolved in the minimum amount of water from which the complex crystallised at room temperature. After a further recrystallisation from water, the orange-yellow crystals were washed twice with alcohol and dried at room temperature. The anhydrous salt was obtained by drying (1 hr.) the powdered crystals to constant weight at 85—90° {loss, 8·7%. Calc. for $Na_2[RuOH(NO_2)_4NO],2H_2O$: 8·7%}. Drying at 110° (cf. ref. 8) caused slight decomposition, shown by a shoulder on the infrared absorption band of the nitrosyl group.

The deuterated analogues were obtained by dissolving the anhydrous salt in 99·7% D_2O and crystallising the product in a desiccator over phosphorus pentoxide; the crystals were removed and dried with filter paper in a dry-box. D_2O of crystallisation was removed by storing the powdered material over phosphorus pentoxide for a few days.

Nitrosylruthenium hydroxide. Separate preparations were made from solutions of nitrosylruthenium complexes in N-hydrochloric, nitric, and sulphuric acid. The previous procedure [8] was modified by continuous centrifugation and readjustment of pH in order to obtain a good yield without recourse to long storage. The precipitates were washed three times each with water (adjustment to pH ~6 to prevent peptisation), alcohol, and acetone, and dried at room temperature [Found: Ru, 47·6; H_2O, 16·1 from chloride solution; Ru, 47·5; H_2O, 16·5 from nitrate solution; Ru, 48·0; H_2O, 17·5 from sulphate solution. $RuNO(OH)_3,2H_2O$ requires Ru, 46·4; H_2O, 16·5%]. Previous preparations [7,8] dried at 80° have indicated one molecule of water per ruthenium atom (49—49·8% of Ru). Deuteration was carried out by suspending the solid in D_2O and drying the product over phosphorus pentoxide in a desiccator.

Hydroxotetra-amminenitrosylruthenium chloride. Material supplied by Johnson Matthey & Co. Ltd. was used {Found: Ru, 35·3. Calc. for $[RuOH(NH_3)_4NO]Cl_2$: Ru, 35·2%}. Deuteration was carried out as for the hydroxide.

The author thanks Mr. A. M. Deane for advice, and Dr. J. M. Fletcher for discussions.

Chemistry Division, Atomic Energy Research Establishment,
Harwell, near Didcot, Berks. [*Received, March* 22*nd*, 1961.]

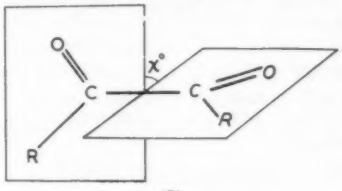
[7] Brown, *J. Inorg. Nuclear Chem.*, 1960, **13**, 73.
[8] Fletcher, Jenkins, Lever, Martin, Powell, and Todd, *J. Inorg. Nuclear Chem.*, 1955, **1**, 378.

876. *Molecular Polarisability: the Conformations of Biacetyl, Benzil, and Furil as Solutes in Benzene or Carbon Tetrachloride.*

By (Miss) P. H. Cureton, (Mrs.) C. G. Le Fèvre, and R. J. W. Le Fèvre.

Measurements of dipole moments, refractivities, molar Kerr constants, etc., of the molecules named in the title, and of phenanthraquinone and furfuraldehyde, indicate that the effective (or average) conformations of biacetyl, benzil, and furil are non-planar (as in I) with azimuthal angles χ^0 *ca.* 160°, 97°, and 118·5° respectively. The phenyl or furyl groups may be twisted about the Ph–(CO) or (C_4H_3O)–(CO) bonds by 5° in the former, or 1° in the latter, case. Data for furfuraldehyde are consistent with the *s-trans*-conformation (II).

In 1939 Caldwell and Le Fèvre [1] suggested that " the stable configuration of benzil in non-polar solvents is one in which the ketonic groups, with their appropriate bonds, are effectively situated in, or make rotational oscillations of low amplitude about, two planes which are roughly mutually perpendicular " (see I). Their evidence was drawn from dipole-moment measurements plus the fact that benzil showed a strong negative Kerr effect in contrast to the small or large positive effects expected respectively for the planar *cis*- or *trans*-variant of (I). Only the molar Kerr constants of benzene and phenanthraquinone have so far been published; [2] this paper now presents the missing observational details and extends the inquiry to biacetyl and furil.



(I)

Experimental

Solutes.—Benzil and furil, prepared from benzaldehyde or furfuraldehyde by standard methods,[3] had m. p. 94—95° and 165—166° (from carbon tetrachloride or methanol respectively). Biacetyl (from L. Light) was dried ($CaCl_2$, then $MgSO_4$) before distillation at 20 mm.; a small quantity, purified through the orthophosphoric acid complex,[4] gave the same dielectric constant increments in both benzene and carbon tetrachloride as the main material. Phenanthraquinone, recrystallised from ethanol, had m. p. 205°. Furfuraldehyde, when required for measurements, was dried ($MgSO_4$) and redistilled immediately before the solutions were made up.

Solvents, Apparatus, and Methods.—Benzene and carbon tetrachloride were as specified in ref. 5, p. 45. Dielectric constants have been determined with the apparatus described in ref. 6, electric double refractions by that in ref. 2, pp. 274—280, or ref. 7, pp. 2462—2481. Procedures for calculating total polarisations at infinite dilution, ${}_\infty P_2$, and molar Kerr constants at infinite dilution, ${}_\infty({}_mK_2)$, from measurements of the dielectric constants, ε_{12}, densities, d_{12}, refractive indexes, n_{12}, and Kerr constants B_{12}, for a solution containing a weight fraction w_2 of solute, are explained in refs. 2, 5, and 7, wherein also other symbols used here are defined. (Subscript 1 indicates solvent, 2 indicates solute, and 12 indicates solution.)

Measurements and Results.—The differences observed between solution and solvent for the various properties are recorded in Table 1, where, *e.g.*, $\Delta\varepsilon$ signifies $\varepsilon_{12} - \varepsilon_1$, ΔB signifies $B_{12} -$

[1] Caldwell and Le Fèvre, *J.*, 1939, 1614.
[2] Le Fèvre and Le Fèvre, *Rev. Pure Appl. Chem.*, 1955, **5**, 261.
[3] Vogel, " A Text-Book of Practical Organic Chemistry," Longmans Green and Co., London, 1948, pp. 678—679, 795.
[4] Olivier, *Bull. Soc. chim. France*, 1932, **51**, 99.
[5] Le Fèvre, " Dipole Moments," Methuen, London, 3rd edn., 1953.
[6] Buckingham, Chau, Freeman, Le Fèvre, Rao, and Tardif, *J.*, 1956, 1405.
[7] Le Fèvre and Le Fèvre, in " Physical Methods of Organic Chemistry," Part 3 of " Technique of Organic Chemistry," ed. A. Weissberger, Interscience Publ., Inc., New York, 3rd edn., 1960.

XUM

TABLE 1. *Increments of dielectric constant, density, Kerr constant, etc., of solvents due to concentrations w_2 of solute.*

Biacetyl in carbon tetrachloride at 25°

$10^6 w_2$	1943	8681	10,192	13,257	18,262	22,683	28,610	38,826
$10^4 \Delta\varepsilon$	58	179	201	267	319	445	525	758
$-10^5 \Delta d$	224	922	—	1410	1947	—	3046	—
$-10^4 \Delta n$	6	16	—	21	26	—	38	53
$10^6 w_2$	6265	8085	12,030	13,845	17,302	19,199		
$-10^{10} \Delta B$ ...	11	13	23	26	32	35		

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 1{\cdot}932$; $\Sigma\Delta d/\Sigma w_2 = -1{\cdot}067$; $\Sigma\Delta n/\Sigma w_2 = -0{\cdot}146_6$; $\Sigma\Delta B/\Sigma w_2 = -1{\cdot}82_5 \times 10^{-7}$; and $\Sigma(n_{12}^2 - n_1^2)/\Sigma w_2 = -0{\cdot}430$.

Biacetyl in benzene at 25°

$10^6 w_2$	5090	5271	6434	9844	10,480	15,336	21,495	21,730	27,362	29,680
$10^4 \Delta\varepsilon$	65	—	—	110	—	169	252	—	316	—
$10^5 \Delta d$	—	33	46	—	69	—	—	140	—	207
$10^6 w_2$	10,776	21,086	29,037	40,165						
$-10^4 \Delta n$	15	25	33	49						
$10^6 w_2$	15,336	21,113	21,495	27,362	29,434	33,998	41,691			
$-10^{10} \Delta B$ ...	33	36	40	51	57	68	78			

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 1{\cdot}153$; $\Sigma\Delta d/\Sigma w_2 = 0{\cdot}0673$; $\Sigma\Delta n/\Sigma w_1 = -0{\cdot}120_7$; $\Sigma\Delta B/\Sigma w_2 = -1{\cdot}90_6 \times 10^{-7}$; and $\Sigma(n_{12}^2 - n_1^2)/\Sigma w_2 = -0{\cdot}3557$.

Benzil in carbon tetrachloride at 20°

$10^5 w_2$	175	671	1063	1174	2023	2496
$-10^{10} \Delta B$ ...	71	216	292	348	554	720

whence $10^7 \Delta B = -29{\cdot}5 w_2 + 0{\cdot}05 w_2^2$.

Benzil in benzene at 25°

$10^5 w_2$	699	2061	2370	2795	2981	3638
$-10^{10} \Delta B$ ...	119	316	367	416	449	646

whence $\Sigma\Delta B/\Sigma w_2 = -15{\cdot}9_6$.

Phenanthraquinone in benzene at 20°

$10^5 w_2$	31	34	76	112	149
$10^{10} \Delta B$ ...	21·5	27	56	78	105

whence $\Sigma(w_2 \,.\, \Delta B)/\Sigma w_2^2 = 70{\cdot}9 \times 10^{-7}$.

Furil in benzene at 25°

$10^6 w_2$	1481	1741	3550	3843	4477	4599	5715	7346	8526	8782
$10^4 \Delta\varepsilon$	101	105	211	218	287	276	346	448	511	546
$10^6 w_2$	1978	3087	3373	4395	6634					
$10^5 \Delta d$ ...	56	92	101	130	192					
$10^6 w_2$	1344	2552	4201	4914	5248	5269	6563	7096	7819	
$-10^{10} \Delta B$ ...	21	43	66	89	91	94	104	117	137	
$10^6 w_2$	4049	5402	7197	7884						
$10^4 \Delta n$ ...	3	4	5	6						

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 6{\cdot}091$; $\Sigma\Delta d/\Sigma w_2 = 0{\cdot}2933$; $\Sigma\Delta B/\Sigma w_2 = -16{\cdot}93 \times 10^{-7}$; $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}073_4$, and $\Sigma(n_{12}^2 - n_1^2)/\Sigma w_2 = 0{\cdot}2160$.

Furfuraldehyde in carbon tetrachloride at 25°

$10^6 w_2$	4045	4672	13,019	31,026
$10^4 \Delta\varepsilon$	983	1148	3236	8016
$10^4 \Delta n$ ...	3	4	9	26
$10^6 w_2$	9818	2015	2385	3207
$-10^5 \Delta d$	612	1222	1563	1958

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 25{\cdot}36_5$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}623_5$; $\Sigma(n_{12}^1 - n_1^2)/\Sigma w_2 = 0{\cdot}2331$.

Furfuraldehyde in benzene at 25°

$10^6 w_2$	2685	4666	5290	6615	9245	10,549
$10^{10} \Delta B$ ...	102	186	216	292	368	439

whence $\Sigma\Delta B/\Sigma w_2 = 41{\cdot}05 \times 10^{-7}$.

B_1, etc. When $w_2 = 0$, we have, for ε_1, d_1, $(n_D)_1$, B_1, etc., and the various constants which enter calculations leading to Table 2, the following:

	ε_1	d_1	$(n_D)_1$	B_1	p_1 (c.c.)	C	H	J	$10^{14}{}_sK_1$
Benzene 20°	2·2825	0·8791	1·5010	0·424	—	—	2·119	0·4670	7·72
,, 25°	2·2725	0·8738	1·4973	0·410	0·34086	0·18809	2·114	0·4681	7·56
CCl_4 20°	2·2360	1·5940	1·4604	0·072	—	—	2·064	0·4721	0·761
,, 25°	2·2270	1·5845	1·4574	0·070	0·18319	0·10596	2·060	0·4731	0·749

Discussion

Dipole Moment of Biacetyl.—The present measurements on biacetyl are reconcilable with those made on the vapour by Bloom and Sutton [8] which showed the resultant moment to rise from 1·05 D at 55° to 1·27 D at 205°. Zahn [9] had previously also reported an increase, 1·25 to 1·48 D, over the temperature range 66° to 231°. Biacetyl has here been examined in two solvents (carbon tetrachloride and benzene) because of the high polarity (1·8 D) earlier claimed in benzene by Caldwell and Le Fèvre; [1] since in all details the data in ref. 1 for biacetyl differ from those in Table 1 of this paper, we conclude that Caldwell and Le Fèvre were not working with the pure diketone, and their value should be replaced accordingly. Bloom and Sutton [8] computed the apparent orientation polarisations at five temperatures on the assumption that the distortion polarisation was 22·7 c.c.; the apparent moments so obtained give smooth plots against temperature and suggest, by extrapolation, that μ at 298° K, corresponding to our measurements, might be 0·8—0·9 D. Since an unknown fraction of the total polarisation may be " vibration polarisation," the values of μ given by Bloom and Sutton and in Table 2 must be regarded as upper estimates.

Table 2. *Calculations of polarisations, moments, and molar Kerr constants from Table* 1.

Solute	Solvent	$\alpha\varepsilon_1$	β	γ	δ	$_\infty P_2$ (c.c.)	R_D (c.c.)	μ (D)	$10^{12}{}_\infty({}_mK_2)$
Biacetyl	CCl_4	1·932	−0·673	−0·100	$-26·0_7$	44·0	20·7	$1·0_4$	−16·3
,, ...	C_6H_6	1·153	0·0770	$-0·08_1$	$-4·64_9$	45·8	20·8	$1·0_8$	−27·2
Benzil	CCl_4	12·58 [a]	−0·341 [a]	0·394 [a]	−410	—	—	3·60 [a]	−663
,, ...	C_6H_6	7·66 [a]	0·260 [a]	0·060 [a]	$-38·7_9$	—	—	3·76 [a]	−663
Phenanthraquinone	C_6H_6	$16·81_5$ [a]	0·347 [a]	0·092 [a]	167·2	—	—	5·57 [a]	2570
Furil	C_6H_6	6·091	0·336	0·049	−41·30	260·9	50·2	3·19	−626
Furfuraldehyde ...	CCl_4	$25·36_5$	$-0·393_5$	—	—	282·8	25·5	$3·5_4$	—
,, ...	C_6H_6	15·2 [b]	0·332 [b]	0·047	100·1	—	—	$3·6_3$ [b]	680

[a] From Caldwell and Le Fèvre.[1] [b] From Calderbank and Le Fèvre (*J.*, 1949, 1462).

Table 3. *Molecular and bond polarisabilities.**

	Benzene	Furan	C–H	C–C	C=O
b_1 (or b_L)	$1·12_0$	0·743	0·064	0·099	0·230
b_2 (or b_T)	$1·12_0$	0·889	0·064	0·027	0·140
b_3 (or b_V)	$0·73_8$	0·537	0·064	0·027	0·046
Source ref.	[a]	[b]	2	2	[c]

* Quoted here, and throughout this paper, in units of 10^{-23} c.c.
[a] Aroney and Le Fèvre, *J.*, 1960, 3600. [b] Le Fèvre, Le Fèvre, Rao, and Smith, *J.*, 1959, 1188. [c] Le Fèvre, Le Fèvre, and Rao, *J.*, 1959, 2340.

Anisotropic Molecular and Bond Polarisabilities used.—Table 3 lists the principal polarisabilities (b_1, b_2, and b_3) of benzene and furan, and the longitudinal, transverse, and " vertical " polarisabilities (b_L^{XY}, b_T^{XY}, and b_V^{XY}) of bonds X–Y required for the calculations which follow.

The general approach has been to estimate the azimuthal angle χ from dipole-moment considerations, then to apply relevant information from Table 3 to the indicated appropriate molecular geometry, thus obtaining b_1, b_2, and b_3 for the solute species (b_1 is consistently

[8] Bloom and Sutton, *J.*, 1941, 727.
[9] Zahn, *Phys. Rev.*, 1932, **40**, 291.

XUM

measured along the direction of action of $\mu_{resultant}$), and finally to compute the molar Kerr constant ${}_mK$ expected for the specified conformation, and to compare ${}_mK$ calc. with ${}_mK$ found.

The Conformation of Biacetyl.—Lu Valle and Schomaker [10] reported that electron-diffraction experiments indicated that biacetyl is coplanar, with a *trans*-configuration, although the possibility that it is a mixture containing a small fraction of *cis*-molecules was not excluded. Bloom and Sutton,[8] discussing the temperature dependence of $\mu_{diacetyl}$, leave undecided whether " there be an equilibrium between *cis*- and *trans*-forms or an unusually rigid fixation in the *trans*-configuration," although they " conclude that there is a very strong tendency for the molecule to be planar." Mizushima [11] asserts that crystals of biacetyl contain only the *trans*-configuration.

The fact (Table 2) that, as a solute, biacetyl shows a *negative* molar Kerr constant is qualitatively incompatible with a mixture of planar *cis*- and *trans*-isomers, since each of these should have a *positive* ${}_mK$ (see Table 4). Further, scale drawings involving the bond lengths and angles given by Lu Valle and Schomaker, plus the " Wirkungsradien " of Stuart [12] (which are *less* than those proposed by Pauling [13]), reveal mutual penetrations of *ca.* 0·4 Å by the spheres of the methyl group and the carbonyl-oxygen atom in the flat *trans*-arrangement, and of *ca.* 1·2 Å by the two methyl groups in the *cis*-arrangement. A skew structure is therefore likely to be more stable than either planar form.

The resultant dipole moment of a 1,2-diketone such as (I), with C–C–O and C–C–C angles of 120°, is:

$$\mu_r = \mu_{CO}\cos 30° \, [2(1 + \cos\chi)]^{0.5}$$

An estimate of the μ_{CO} component can be made from the moment of camphorquinone (4·46 D; Le Fèvre, Maramba, and Werner [14]), a molecule in which the carbonyl groups are fixed by attachment in a rigid cage of C–C links. If all angles are accepted as tetrahedral, the two μ_{CO} vectors interact at 70°, so that $\mu_{CO} = 2{\cdot}72$ D. This datum, with $\mu_{diacetyl} = 1{\cdot}08$ D, yields $\chi = 153{\cdot}5°$; polarisabilities, and hence the ${}_mK$ calc., follow as in Table 4. The predicted ${}_mK$ is somewhat too negative; the best compromise, if both μ_r calc. and ${}_mK$

TABLE 4. *Polarisabilities,* dipole moments, and* ${}_mK$*'s expected for biacetyl with various values of the azimuthal angle.*

χ	μ_r (calc.)	b_1	b_2	b_3	$10^{13}{}_mK$ (calc.)
180°	0	0·530	0·898	1·014	+9·59
160	0·82$_1$	0·569	,,	0·975	−20·4
153·5	1·08	0·579	,,	0·965	−39·0
140	1·62	0·607	,,	0·937	−84·9
120	2·36	0·664	,,	0·880	−136·6
100	3·04	0·734	0·898	0·810	−122·0
0	4·73	1·014	,,	0·530	+749·5

* b_1 is measured parallel to μ_r in all cases where μ_r is non-zero; the location of b_3 along the central C–C bond is, strictly, valid only when $\chi = 0°$, but errors thus introduced are small: when $\chi = 180°$, b_3 will deviate from the C–C line to the maximum extent; calculation, by the method explained in ref. 7, p. 2486, with $b_{zz} = 0{\cdot}898$, $b_{yy} = 1{\cdot}014$, and $b_{zz} = 0{\cdot}530$, gives the principal polarisabilities as 0·896, 1·016, and 0·530, with the first of these located 7° 24′ from the C–C bond. The argument, that for this non-polar conformation ${}_mK$ will be algebraically positive, is not affected.

calc. are considered, is a conformation with $\chi = ca.\ 160°$. Since, near $\chi = 160°$, the rates of change of μ_r and ${}_mK$ with χ are linear and non-linear respectively, the greater differences (Table 2) between the ${}_mK$s than between the apparent moments in benzene and carbon tetrachloride could be partly due to biacetyl's having a greater amplitude of vibration in

[10] Lu Valle and Schomaker, *J. Amer. Chem. Soc.*, 1939, **61**, 3520.
[11] Mizushima, " Structure of Molecules and Internal Rotation," Academic Press, Inc., New York, 1954, p. 75.
[12] Stuart, *Z. phys. Chem.*, 1935, *B*, **27**, 350.
[13] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, New York, 2nd edn., 1945, p. 189.
[14] Le Fèvre, Maramba, and Werner, *J.*, 1953, 2496.

XUM

the former medium than in the latter. Consistently with the suggestion made above, that Sutton's " vibration polarisation " contributes to the measured ${}_{\infty}P_2$, we note that the ${}_{\infty}P_2$ in benzene slightly exceeds that in carbon tetrachloride.

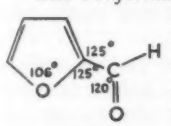
The Conformation of Benzil.—As with biacetyl the negativity of the ${}_{m}K$ observed eliminates the possibility that benzil as a solute exists as a mixture of planar *cis*- and *trans*-isomers, the ${}_{m}K$'s of which would be positive; phenanthraquinone can be regarded as a rough substitute for the former conformation. Scale models indicate the likelihood that a skew structure, as proposed in ref. 1, is alone permitted by steric factors. *A priori* calculations of molecular polarisabilities are complicated by ignorance of the degree to which each benzoyl group is itself non-planar.

From $\mu_{\text{phenanthraquinone}} = 5{\cdot}5_7$ D, and from an assumption that C–(CO)–(CO) angles are 120°, μ_{CO} is found to be $3{\cdot}2_3$ D; this, applied to $\mu_{\text{benzil}} = 3{\cdot}7$ D, shows χ to be *ca.* 97°. This value fits the ${}_{m}K$'s now found, provided (*a*) that the phenyl rings are twisted by 5·1° about their Ph–(CO) bonds from flat arrangements of each Ph·C:O moiety, and (*b*) that all C–C–C angles are 120°:

$$b_1 = 1{\cdot}89_0,\ b_2 = 2{\cdot}62_1,\ b_3 = 2{\cdot}03_5,\ {}_{m}K \text{ calc.} = -663 \times 10^{-12}$$

On this basis, agreement between prediction and measurement is very satisfactory.

The Conformation of Furil.—The problem here is similar to that with benzil but more complicated because the furyl group, unlike phenyl, contributes a polarity vector to the resultant molecular dipole moment. The moment of furan [15] is 0·72 D, and of furfuraldehyde 3·5—3·6 D; the latter is close enough to the sum of μ_{furan} and [16] $\mu_{\text{benzaldehyde}}$ to justify adopting for furfuraldehyde the *s-trans* conformation (II) in which μ_r acts approximately parallel to the C=O axis. If the furoyl radicals in furil resemble (II) and carry moment components of $3{\cdot}6_3$ D, χ for furil ($\mu_r = 3{\cdot}1_9$ D) emerges as 118·5°, and



(II)

$$b_1 = 1{\cdot}38_0,\ b_2 = 2{\cdot}09_1,\ b_3 = 1{\cdot}81_6,\ {}_{m}K \text{ calc.} = -626 \times 10^{-12}$$

if the planes of the furyl rings are rotated 1° analogously to the rotations described above for the phenyl group in benzil.

The Conformation of Furfuraldehyde.—If for compound (II) angles are adopted as shown (cf. ref. 17 for furan and acraldehyde), together with previously [18] determined polarisabilities of the bonds involved, b_1 (along the C=O bond), b_2 and b_3 can be predicted as 1·18, 0·90, and $0{\cdot}59 \times 10^{-23}$ respectively; these lead to a calculated molar Kerr constant of 623×10^{-12}, a value somewhat less than that observed (680×10^{-12}). From refractivity measurements [19] the electronic polarisation of furfuraldehyde is 24·06 c.c. whence $b_1 + b_2 + b_3 = 2{\cdot}860 \times 10^{-23}$ c.c. compared with the calculated sum of $2{\cdot}67 \times 10^{-23}$ c.c.; evidently there is an exaltation of polarisability of $0{\cdot}19 \times 10^{-23}$ c.c., but the distribution of this cannot be foreseen *a priori*. We note, however, that if this be equally divided between b_1 and b_2 (so that the semi-axes are $1{\cdot}27_5$, $0{\cdot}99_5$, and $0{\cdot}59 \times 10^{-23}$) the calculated ${}_{m}K$ becomes 686×10^{-12} in good agreement with experiment.

School of Chemistry, The University,
Sydney, N.S.W., Australia.

[*Received, April 4th*, 1961.]

[15] Le Fèvre, Le Fèvre, Rao, and Smith, *J.*, 1959, 1188; Harris, Le Fèvre, and Sullivan, *J.*, 1953, 1622; Buckingham, Harris, and Le Fèvre, *J.*, 1953, 1626.
[16] Calderbank and Le Fèvre, *J.*, 1949, 1462.
[17] *Chem. Soc. Special Publ.*, No. 11, 1958.
[18] Le Fèvre and Le Fèvre, *J.*, 1936, 3549; Bramley, Le Fèvre, Le Fèvre, and Rao, *J.*, 1959, 1183.
[19] Timmermans, " Physico-chemical Constants of Pure Organic Liquids," Elsevier, New York, 1950, p. 501.

877. *Metal–Metal Interactions in Square-planar Complexes.*

By J. R. Miller.

Ten double complex salts of copper, palladium, and platinum are isomorphous with Magnus's green salt, $[Pt(NH_3)_4][PtCl_4]$. Abnormal colours, associated with metal–metal interaction, are restricted to compounds containing platinum in both anion and cation. It is therefore concluded that adoption of the structure is not dependent on metal–metal interaction, and it is shown on simple electrostatic grounds that the structure would be expected to be very stable.

Some of the theories concerning interactions in these compounds and in the comparable *vic*-dioxime complexes of nickel, palladium, and platinum are discussed, and it is suggested that the interaction could be of an anti-bonding nature.

The deep green colour of tetrammineplatinum(II) chloroplatinate(II), Magnus's green salt, has attracted attention for many years; the anion is usually red in salts and solutions, the cation colourless, so the green colour of the combined salt points to some abnormality. In 1932, Cox *et al.*[1] showed that the tetragonal crystal contains chains of alternate square-planar anions and cations stacked flat on top of each other with a separation of 3·21 Å; the ionic planes are perpendicular to the *c*-axis. These authors did not make any suggestions about the source of the unusual colour.

In 1951, Yamada [2] found that the crystal spectrum is very unusual. The absorption maxima of " normal " chloroplatinate(II) and tetrammineplatinum(II) are shifted to lower frequencies and the dichroism is " abnormal," *i.e.*, absorption of light with its electric vector perpendicular to the ionic planes is at a lower frequency and more intense than that of light with electric vector parallel to these planes. One normally finds the reverse situation in the spectra of flat molecules. Yamada concluded that there is some sort of direct interaction between neighbouring platinum atoms.

The first theoretical approach was made by Godycki and Rundle,[3] in a study of bis(dimethylglyoximato)nickel(II). This compound has a structure analogous to Magnus's green salt in that planar molecules are stacked in chains, alternate ones being twisted through 90° to allow a close approach of nickel atoms (3·245 Å). These workers sought an explanation of the specificity of dimethylglyoxime as a gravimetric reagent for nickel and for palladium, and, citing the slight pleochroism of the compound, suggested that there is a bonding interaction between the nickel atoms. This would be of sufficient strength to stabilise the simple packing and to cause the low solubility, in contrast to the very soluble copper compound. They suggested that the bonding could arise from partial excitation of 3*d*-electrons to empty 4*p*-orbitals, with pairing of electrons on neighbouring atoms. Thus the hybridisation would be effectively changed from dsp^2 to d^2sp^3. This theory was supported by the discovery that the dichroism is, in fact, abnormal in a way similar to that of Magnus's green salt.[4] A gold compound, $[Au(DH)_2][AuCl_2]$ (DH_2 = dimethylglyoxime), was found to have a structure [5] analogous to that of bis(dimethylglyoximato)nickel, but was later shown to exhibit normal dichroism.[6]

In 1957, Rundle extended his theory of the interaction by using molecular-orbital theory.[7] The only essential difference was that a copper(II) compound of this structure would have its odd electron in a b_{1g}* orbital (anti-bonding orbital derived from $3d_{x^2-y^2}$), instead of in a 4*p*-orbital. Thus the odd electron of copper(II) would play no part in the

[1] Cox, Pinkard, Wardlaw, and Preston, *J.*, 1932, 2527.
[2] Yamada, *J. Amer. Chem. Soc.*, 1951, **73**, 1579.
[3] Godycki and Rundle, *Acta Cryst.*, 1953, **6**, 487.
[4] Yamada and Tsuchida, *J. Amer. Chem. Soc.*, 1953, **75**, 6351.
[5] Rundle, *J. Amer. Chem. Soc.*, 1954, **76**, 3101.
[6] Yamada and Tsuchida, *Bull. Chem. Soc. Japan*, 1957, **30**, 715.
[7] Rundle, *J. Phys. Chem.*, 1957, **61**, 45.

XUM

interaction, and the earlier notion that copper(II) compounds could not adopt this structure was modified.

At about the same time the crystal structure of Magnus's green salt was re-examined,[8] and a more satisfactory sideways packing of the chains was found. The platinum–platinum distance was corrected to 3·245 Å, exactly the same as the nickel–nickel distance in bis(dimethylglyoximato)nickel.

Sharpe and Wakefield,[9] in a study of a series of *vic*-dioxime complexes, concluded that the solubility does depend on the nickel–nickel distance; their ligands were all similar and may be presumed to have had little effect on solubility differences. Banks and Barnum,[10] in a similar study, used a very much larger range of ligands and found that these differences had a greater effect on the solubility than did variations in the intermetallic distance.

In a second publication,[11] the latter authors described the solution and solid-state spectra of their complexes. They found bands at the long-wavelength ends of the solid-state spectra which were not present in the solution spectra, and they justifiably concluded that these bands were associated with the metal–metal interactions. For an isomorphous series of nickel(II) and palladium(II) complexes, the frequency decreases with decreasing intermetallic distance.

In an attempt to study the effect of increasing intermetallic distance, Yamada and Tsuchida [12] measured the dichroism of alkyl homologues of Magnus's green salt. Only the green compound, $[Pt(Me{\cdot}NH_2)_4][PtCl_4]$, shows abnormal dichroism; higher amines give rise to pink compounds with normal dichoism. The result that compounds of this nature with more or less expected colours show normal dichroism is used extensively in the present study to indicate those cases where interaction does not occur.

Finally, two copper compounds must be mentioned which show direct stacking in their structures; in neither case has the dichroism been examined. First, tetramminecopper(II) chloroplatinate(II) is isomorphous with Magnus's green salt and has a slightly shorter *c*-axis;[13,14] secondly, bis-(*N*-methylsalicylaldiminato)copper(II) has a structure [15] rather similar to that of bis(dimethylglyoximato)nickel,[3] with an interplanar distance of 3·33 Å. It is therefore clear that this type of structure is not confined to ions and molecules of d^8-configuration, and, under the right conditions, it may be much more general.

The object of this study is to examine some of the factors affecting the occurrence of the Magnus's green salt structure and of metal–metal interaction. Some of the results have already been published,[14] but are repeated for completeness.

Results and Discussion

The Table lists the important properties of the compounds examined. All substances are tetragonal except (XII). It is clear that all these compounds, except (XII), have unit cells very similar to that of Magnus's green salt. Close examination of absent reflections and of intensities in the powder photographs indicates that the compounds have the same space-group $P4/mnc$, and therefore, by analogy, the anions and cations are stacked in chains with metal–metal distances of $c/2$.

The green compounds (V, VI, and VIII) are known to be abnormally dichroic;[2,12] it is assumed that (IX) also has this property, but that the remainder are either normal or show very slight interaction. Thus, in the compounds examined, only four of the five containing platinum in both ions show strong interaction; introduction of another metal

[8] Atoji, Richardson, and Rundle, *J. Amer. Chem. Soc.*, 1957, **79**, 3017.
[9] Sharpe and Wakefield, *J.*, 1957, 281.
[10] Banks and Barnum, *J. Amer. Chem. Soc.*, 1958, **80**, 3579.
[11] Banks and Barnum, *J. Amer. Chem. Soc.*, 1958, **80**, 4767.
[12] Yamada and Tsuchida, *Bull. Chem. Soc. Japan*, 1958, **31**, 813.
[13] Bukovska and Porai-Koshits, *Kristallografiya*, 1960, **5**, 137.
[14] Miller, *Proc. Chem. Soc.*, 1960, 318.
[15] Lingafelter, Morosin, and Simmons, *Acta Cryst.*, 1960, **13**, 1025.

removes it, without appreciably changing the lattice constants. Close similarity of bond lengths is of common occurrence in corresponding palladium and platinum compounds, and interaction in the all-platinum salts is not sufficient to disturb this.

Substitution of methylamine for ammonia in the salts has no effect on the length of the *c*-axis, indicating that the methyl groups are held in the platinum–nitrogen plane, and that the structure is strong enough to prevent rotation about the platinum–nitrogen bonds. Models show that ethylamine is too large to fit into the plane, and the ethylamine complex has a totally different structure from Magnus's green salt; this fits in well with the pink colour and the " normal " dichroism.[12] (It should be pointed out that the choice of axis in the dichroism measurements on this compound may have been in error, but this would not affect the issue as in any case no large shift was observed.)

Compound (XI) occupies a special place in the scheme. The metal–metal distance is 3·35 Å, only very slightly greater than the longest to be found among the abnormal compounds [3·31 Å in (VIII)], and so, when the small spectroscopic difference between red and green is borne in mind, it may well be that this compound shows a weakly abnormal dichroism. Attempts were made to correlate the interplanar distances with the known dichroism [2,12] of compounds (V, VI, and VIII), but this was not very informative as the spectra seem to have been measured in slightly different regions. Remarkably, the shift of the perpendicular absorption is greater for the bromide (VIII) than for Magnus's green salt; the former has a longer *c*-axis, and so it seems that the ligand, as well as the metal–metal distance, must have an effect on the interaction. A complete investigation of the crystal spectra of compounds (IX and XI) is required.

The magnetic susceptibility of compound (III) was measured down to liquid-nitrogen temperatures; it obeyed the Curie–Weiss law with a Weiss constant of only 13°, giving $\mu_{eff.} = 1{\cdot}90$ B.M. Thus copper–platinum interaction is ruled out in this temperature

Compound		Colour	Expected colour	*a* (Å)	*c* (Å)
$[Pd(NH_3)_4][PdCl_4]$	I	Pink	Pink	8·96	6·49
$[Pt(NH_3)_4][PdCl_4]$	II	Pink	Pink	8·98	6·45
$[Cu(NH_3)_4][PtCl_4]$	III	Purple	Purple	9·07 9·06 [13]	6·46 6·43 [13]
$[Pd(NH_3)_4][PtCl_4]$	IV	Pink	Pink	9·00	6·50
$[Pt(NH_3)_4][PtCl_4]$	V	Green	Pink	8·96 9·03 [8]	6·46 6·50 [8]
$[Pt(Me{\cdot}NH_2)_4][PtCl_4]$	VI	Green	Pink	10·35	6·49
$[Pd(NH_3)_4][PdBr_4]$	VII	Red	Red	9·32	6·66
$[Pt(NH_3)_4][PtBr_4]$	VIII	Green	Red	9·32	6·62
$[Pt(Me{\cdot}NH_2)_4][PtBr_4]$	IX	Green	Red	10·55	6·61
$[Pd(NH_3)_4][Pd(SCN)_4]$	X	Pink	Pink	10·60	6·69
$[Pt(NH_3)_4][Pt(SCN)_4]$	XI	Red	Orange	10·62	6·70
$[Pt(Et{\cdot}NH_2)_4][PtCl_4]$	XII	Pink	Pink	Not tetragonal	

range; it must, however, be remembered that the odd electron is in the b_{1g}*-orbital, which is not suitable for interaction, being localised in the copper–ammonia plane. If a complex ion of cobalt(II), for example, were found in a similar environment, there would be a good chance of finding anomalous magnetic behaviour, as the odd electron would lie in the all-important a_{1g}*-orbital ($3d_{z^2}$ with some intermixing of 4*s*).

It has been suggested that the metal–metal interaction is responsible for the adoption of this structure, and for the low solubility of Magnus's green salt.[3,8] Whilst no quantitative solubility measurements have been carried out, it is worth noting that the pink compounds (I—IV) are insoluble, whilst the green compounds (VI and IX) are moderately soluble in water (giving red solutions). Solubility depends on the difference between lattice energy and heats of solvation. By applying the relationship,[16] $U_c = 2Nz^2e^2 \ln 2/d$, for the Coulombic lattice energy of a chain of positive and negative charges,

[16] Moelwyn-Hughes, " Physical Chemistry," Pergamon Press, London, 1957.

values of U_c from −575 to −550 kcal./mole are obtained as d varies from 3·20 to 3·35 Å. These are in all probability lower than the true lattice energies, as sideways attractions between charges have been neglected. They are much higher than those of the alkali-metal halides, and somewhat smaller than those of the insoluble oxides and sulphides of bivalent metals.[17] Since the flat complex ions are considerably larger than alkaline-earth, oxide, or sulphide ions, they would be expected to have smaller heats of solvation. It follows that low solubility is to be expected, and that the Magnus's green salt structure is particularly stable, regardless of the existence of any metal–metal interactions.

Theory of Interaction.—There are three types of compound which form "direct-stacking" structures. First, there are the well-established organic addition complexes such as quinhydrone, which consists of chains of alternate quinone and quinol molecules stacked in parallel,[18] with an interplanar spacing of 3·16 Å. The dichroism is strongly abnormal,[19] and the properties can be readily interpreted as due to co-ordination of the quinol π-electrons to the empty π-orbitals of the quinone. The fact that hexamethylbenzene,[20] for example, does not form quite such a simple structure may be put down to repulsion of the π-electrons.

The second type of compound consists of the *vic*-dioximates of nickel, palladium, and platinum, and bis-(*N*-methylsalicylaldiminato)copper(II). Abnormal dichroism is apparent in the nickel and platinum dimethylglyoxime complexes.[4] This cannot be ascribed to a charge-transfer mechanism as in quinhydrone, because neighbouring molecules are identical. In Rundle's theory [7] interaction between only two molecules is considered, but this theory may be readily extended to cover a chain of n molecules. The a_{1g}*- and the $a_{2u}(4p_z)$-orbitals each form a bonding and an anti-bonding band; those from the a_{1g}*-orbitals are fully occupied, and without further treatment it can be seen that the net result would be anti-bonding. Rundle suggested that configurational interaction between the anti-bonding a_{1g}*- and the bonding a_{2u}-bands would give the modification required to lower the energy. Such interaction would presumably give a function which allowed the highest-energy electrons considerable freedom of movement along the chain.

An alternative presentation is to allow the a_{1g}*- and the a_{2u}-orbitals on one molecule to form two equivalent hybrids; each would have a large lobe along the axis. When a chain of n molecules is formed, the hybrids give rise to two non-bonding orbitals, $n - 1$ equivalent bonding and $n - 1$ equivalent anti-bonding orbitals. If n is large, the non-bonding orbitals, which are at each end of the chain, may be neglected. The electrons fill the bonding orbitals and half-occupy the non-bonding orbitals, and so the overall effect would be bonding.

There is the further possibility that the anti-bonding band from a_{1g}* can reach above the b_{1g}* level, which is intermediate between a_{1g}* and a_{2u} in an isolated molecule. In this case, half of the axial electrons would be forced into the b_{1g}*-orbitals in the planes of the molecules, while the other half would be stabilised along the axis.

Banks and Barnum [11] attributed the band in the solid-state spectra of their dioxime complexes to a transition from a_{1g}* to b_{1g}*. In order to account for the *drop* in frequency with decreasing metal–metal distance, one must assume that the gap between a_{1g}* and b_{1g}* becomes smaller as the metal–metal distance decreases. This could come about very simply by interaction of the a_{1g}*-orbitals alone, the a_{2u}-orbitals being neglected; these orbitals would interact to form an energy band, which would have an overall anti-bonding effect, since all levels are occupied. In such a case, the structure would be formed in spite of the interaction, rather than on account of it.

By combining the two extremes, of interaction between the a_{1g}*-orbitals alone and of

[17] Waddington, "Advances in Inorganic Chemistry and Radiochemistry," Academic Press, 1959, Vol. I.
[18] Matsuda, *Bull. Chem. Soc. Japan*, 1958, **31**, 611.
[19] Nakamoto, *J. Amer. Chem. Soc.*, 1952, **74**, 1739.
[20] Robertson, "Organic Crystals and Molecules," Cornell Univ. Press, 1953.

hybridisation of a_{1g}* and a_{2u}, it is seen that the amount of bonding or anti-bonding would depend on the exact amount of mixing of the a_{2u}- into the a_{1g}*-orbitals.

Compounds with the composition of Magnus's green salt form the third class. In this case the co-ordination theory applicable to quinhydrone is equivalent to the molecular-orbital theory, as neighbouring species are not identical. Co-ordination could be considered to occur from the a_{1g}* of the anion to the a_{2u} of the cation. The exact reason why palladium compounds do not seem to have this interaction must lie in the relative sizes of the orbitals concerned, or it may be that platinum can use its 4*f*-orbitals to advantage.

The conclusion to be drawn from this work is that metal–metal interaction cannot be held responsible for the adoption of the Magnus's green salt structure, but rather that such interaction can occur in certain compounds which crystallise in this way. The Magnus's green salt structure is an electrostatically favourable one for doubly-charged square-planar ions to adopt, without the influence of these interactions which at present seem to be limited to platinum–platinum salts with intermetallic distances less than 3·35 Å. Present indications are that several other materials crystallise in slightly deformed versions of the Magnus's green salt lattice, and this can be explained by repulsion of π- and a_{1g}*-electrons. It is suggested that the analogous structures of *vic*-dioxime complexes may be explained in terms of favourable packing, and that when metal–metal interaction occurs, the possibility of its being anti-bonding should not be excluded.

Experimental

Compounds were obtained as crystalline precipitates by mixing stoicheiometric amounts of the appropriate ions in aqueous solution. The solutions were cooled to 0° before mixing to avoid formation of monomers such as dichlorodiamminepalladium and to discourage exchanges of ligand between different metal atoms. Acid was added, where it did not react with the cation, as this is reputed to encourage the formation of green compounds.[1] The analyses are listed.

Tetramminepalladium chloropalladate(II). Found: Pd, 49·8; Cl, 32·9. Calc. for $H_{12}Cl_4N_4Pd_2$: Pd, 50·3; Cl, 33·6%.

Tetrammineplatinum chloropalladate(II). Found: Pd, 20·4; Cl, 27·4. Calc. for $H_{12}Cl_4N_4PdPt$: Pd, 20·8; Cl, 27·7%.

Tetramminepalladium chloroplatinate(II). Found: Pd, 20·6; Cl, 27·6%.

Tetramminecopper chloroplatinate(II). Found: N, 12·3; Cl, 30·4. Calc. for $H_{12}Cl_4CuN_4Pt$: N, 11·95; Cl, 30·25%.

Tetrammineplatinum chloroplatinate(II). Found: Cl, 23·5. Calc. for $H_{12}Cl_4N_4Pt_2$: Cl, 23·6%.

Tetramminepalladium bromopalladate(II). Found: Pd, 34·8; Br, 53·4. Calc. for $H_{12}Br_4N_4Pd_2$: Pd, 35·5; Br, 53·2%.

Tetrammineplatinum bromoplatinate(II). Found: Br, 40·8. Calc. for $H_{12}Br_4N_4Pt_2$: Br, 41·1%.

Tetramminepalladium thiocyanatopalladate(II). Found: Pd, 40·8; SCN, 45·0. Calc. for $C_4H_{12}N_8Pd_2S_4$: Pd, 41·5; SCN, 45·2%.

Tetra(methylamine)platinum chloroplatinate(II). Found: C, 6·7; H, 3·1; N, 9·05; Cl, 21·6. Calc. for $C_4H_{20}N_4Cl_4Pt_2$: C, 7·3; H, 3·1; N, 8·5; Cl, 21·6%.

Tetra(methylamine)platinum bromoplatinate(II). Found: C, 5·1; H, 2·4; N, 6·1; Br, 38·4. $C_4H_{20}Br_4N_4Pt_2$ requires C, 5·8; H, 2·4; N, 6·7; Br, 38·3%.

Tetra(ethylamine)platinum chloroplatinate(II). Found: C, 13·0; H, 3·3; N, 8·1; Cl, 19·9. Calc. for $C_8H_{28}Cl_4N_4Pt_2$: C, 13·5; H, 4·0; N, 7·9; Cl, 19·9%.

X-Ray Powder Photographs.—These were taken in Unicam 19 cm. cameras, with Cu-$K\alpha$ radiation. The finely powdered samples were packed into thin-walled Pyrex glass capillaries, which were sealed with picein wax. The $\sin^2\theta$ values and the indexing are tabulated. The unit cell dimensions are listed in the discussion section.

Magnetic Susceptibility.—The susceptibility of $[Cu(NH_3)_4][PtCl_4]$ was measured by the Gouy method in the temperature range 83—293° K. It obeyed the equation $\chi_M = \mu_{eff.}^2/2{\cdot}84^2(T + 13)$, where $\mu_{eff.} = 1{\cdot}90$ B.M.

Int.	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	*hkl*
	$[Pd(NH_3)_4][PdCl_4]$		
vs	0·0144	0·0148	110
s	0·0293	0·0295	200
w	0·0501	0·0510	211
s	0·0559	0·0564	002
s	0·0706	0·0712	112
s	0·0735	0·0738	310
ms	0·0856	0·0859	202
ms	0·0874	0·0879	311
ms	0·1176	0·1180	400
ms	0·1296	0·1302	312
w	0·1325	0·1328	330
ms	0·1469	0·1475	420
ms	0·1738	0·1744	402
mw	0·1889	0·1892	332
mw	0·1918	0·1918	510
	$[Pd(NH_3)_4][PtCl_4]$		
vs	0·0144	0·0147	110
mw	0·0211	0·0214	101
m	0·0290	0·0293	200
m	0·0561	0·0562	002
m	0·0708	0·0708	112
m	0·0729	0·0734	310
vw	0·0798	0·0801	301
m	0·0860	0·0856	202
w	0·1169	0·1174	400
mw	0·1296	0·1296	312
mw	0·1468	0·1468	420
mw	0·1736	0·1738	402
w	0·1894	0·1883 0·1908	332 510
m	0·2036	0·2030	422
w	0·2491	0·2496	530
	$[Pt(NH_3)_4][PdCl_4]$		
vs	0·0143	0·0148	110
s	0·0286	0·0296	200
vw	0·0366	0·0370	210
w	0·0517	0·0513	211
s	0·0565	0·0572	002
s	0·0719	0·0720	112
s	0·0741	0·0740	310
m	0·0869	0·0868	202
w	0·1182	0·1184	400
ms	0·1312	0·1312	312
m	0·1481	0·1480	420
mw	0·1759	0·1756	402
w	0·1926	0·1924	510
m	0·2054	0·2052	422
w	0·2498	0·2516	530

Int.	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	$\sin^2\theta$ (*R*)	*hkl*
		$[Pt(NH_3)_4][PtCl_4]$		
m	0·0140	0·0142	0·0141	001
s	0·0150	0·0148	0·0146	110
m	0·0298	0·0296	0·0292	200
mw	0·0572	0·0570	0·0564	002
mw	0·0595	0·0592	0·0583	220
mw	0·0722	0·0718	0·0710	112
s	0·0743	0·0740	0·0729	310
mw	0·0869	0·0866	0·0856	202
ms	0·1187	0·1184	0·1166	400
m	0·1309	0·1310	0·1293	312
m	0·1332	0·1332	0·1312	330
s	0·1481	0·1480	0·1458	420
m	0·1753	0·1754	0·1731	402
m	0·1922	0·1924	0·1895	510
ms	0·2043	0·2050	0·2022	422

$\sin^2\theta$ (*R*) values are calculated from the unit cell of Atoji *et al.*[5]

Int.	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	$\sin^2\theta$ (*B*)	*hkl*
		$[Cu(NH_3)_4][PtCl_4]$		
vs	0·0142	0·0145	0·0145	110
s	0·0213	0·0215	0·0216	101
s	0·0290	0·0289	0·0290	200
w	0·0500	0·0504	0·0506	211
s	0·0568	0·0570	0·0575	002
vs	0·0719	0·0715 0·0723	0·0720 0·0724	112 310
mw	0·0795	0·0793	0·0796	301
s	0·0862	0·0859	0·0865	202
w	0·1083	0·1082	0·1085	321
m	0·1157	0·1157	0·1159	400
ms	0·1297	0·1293 0·1304	0·1299 0·1301	312 330
mw	0·1369	0·1372	0·1375	411
m	0·1451	0·1446	0·1448	420
m	0·1729	0·1727	0·1734	402
m	0·1881	0·1871 0·1880	0·1879 0·1883	332 510
w	0·1949	0·1950	0·1954	431
ms	0·2022	0·2016 0·2022	0·2024 0·2027	422 511

$\sin^2\theta$ (*B*) values are calculated from the unit cell in ref. 13.

Int.	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	*hkl*
	$[Pd(NH_3)_4][PdBr]$		
s	0·0135	0·0137	110
w	0·0201	0·0202	101
ms	0·0272	0·0274	200
w	0·0345	0·0343	210
m	0·0476	0·0477	211
s	0·0534	0·0536	002
ms	0·0673	0·0673	112
ms	0·0687	0·0685	310
ms	0·0817	0·0810 0·0819	202 311
m	0·1096	0·1096	400
m	0·1221	0·1221	312
m	0·1371	0·1370	420
m	0·1633	0·1632	402
vw	0·1702	0·1700	412
vw	0·1788	0·1769 0·1781	332 510
mw	0·1908	0·1906	422
mw	0·2467	0·2466	600
	$[Pt(NH_3)_4][PtBr_4]$		
vs	0·0132	0·0137	110
vw	0·0201	0·0204	101
s	0·0272	0·0274	200
vw	0·0337	0·0342	210
mw	0·0475	0·0478	211
s	0·0539	0·0542	002
vs	0·0681	0·0685	310
s	0·0815	0·0816	202
m	0·1094	0·1096	400
s	0·1227	0·1227	312
vw	0·1297	0·1300	411
m	0·1371	0·1370	420
m	0·1638	0·1638	402
vw	0·1712	0·1706 0·1712	412 430
m	0·1781	0·1775 0·1781	332 510
vw	0·1848	0·1848	431
ms	0·1916	0·1912	422
	$[Pd(NH_3)_4][Pd(SCN)_4]$		
vs	0·0105	0·0106	110
w	0·0186	0·0186	101
s	0·0210	0·0212	200
vw	0·0399	0·0398	211
vw	0·0423	0·0423	220
vs	0·0531	0·0529 0·0531	310 002
s	0·0636	0·0637	112
ms	0·0743	0·0743	202
m	0·0820	0·0821	321

Int.	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	*hkl*
	$[Pd(NH_3)_4][Pd(SCN)_4]$.		
m	0·0953	0·0952 0·0954	330 222
s	0·1062	0·1058 0·1060	420 312
ms	0·1377	0·1375 0·1378	510 402
m	0·1483	0·1483	332
ms	0·1593	0·1589	422
m	0·1689	0·1693	440
	$[Pt(NH_3)_4][Pt(SCN)_4]$		
vs	0·0105	0·0106	110
vw	0·0188	0·0185	101
s	0·0211	0·0211	200
w	0·0423	0·0422	220
vs	0·0529	0·0528 0·0529	310 002
mw	0·0634	0·0635	112
vw	0·0822	0·0818	321
w	0·0844	0·0844	400
mw	0·0951	0·0950 0·0951	330 222
s	0·1059	0·1055 0·1057	420 312
m	0·1379	0·1372 0·1373	510 402
w	0·1591	0·1584	422
w	0·1700	0·1688	440
mw	0·1793	0·1793	530
mw	0·1903	0·1899 0·1901	600 512
mw	0·2115	0·2110 0·2116	620 004
	$[Pt(MeNH_2)_4][PtCl_4]$		
vs	0·0109	0·0111	110
s	0·0220	0·0222	200
m	0·0444	0·0444	220
s	0·0558	0·0555 0·0564	310 002
ms	0·0675	0·0675	112
vw	0·0691	0·0696	311
m	0·0783	0·0786	202
mw	0·0886	0·0888	400
s	0·1003	0·0999 0·1008	330 222
vs	0·1114	0·1110 0·1119	420 312
ms	0·1447	0·1442 0·1452	510 402
m	0·1564	0·1563	332
s	0·1676	0·1674	422
w	0·1779	0·1775	440
mw	0·1889	0·1886	530
m	0·2008	0·1997 0·2006	600 512
ms	0·2783	0·2783	622
	$[Pt(MeNH_2)_4][PtBr_4]$		
vs	0·0105	0·0107	110
vw	0·0189	0·0189	101
m	0·0212	0·0214	200
w	0·0425	0·0427	220
s	0·0541	0·0544	002
vw	0·0614	0·0617	301
s	0·0647	0·0651	112
m	0·0756	0·0758	202
w	0·0852	0·0854	400
m	0·0963	0·0961 0·0971	330 222
s	0·1070	0·1068 0·1078	420 312
m	0·1383	0·1388	510
m	0·1507	0·1505	332
s	0·1611	0·1612	422
w	0·1814	0·1816	530
m	0·1934	0·1932	512

I am indebted to Dr. D. Machin, of University College, London, for the magnetic susceptibility of tetramminecopper chloroplatinate(II), and also thank Drs. A. G. Sharpe and T. C. Waddington for help and discussion, and the D.S.I.R. for a maintenance grant.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, April 10th*, 1961.]

878. *Thermodynamics of Ion Association. Part IX.*[1] *Some Transition-metal Succinates.*

By A. McAuley and G. H. Nancollas.

E.m.f.s of cells of the type H_2, Pt|H_2A, NaOH, MCl_2|AgCl/Ag, where H_2A represents succinic acid, measured by a precision method at temperatures from 0° to 45°, are interpreted in terms of the formation of NiA, CoA, and MnA, and the corresponding hydrogen succinates, $NiHA^+$ and $MnHA^+$. Preliminary pH measurements, in which a glass electrode was used, at a constant ionic strength (0·2M) were used to identify the ion-pairs present in the solutions. ΔH, ΔG, ΔS, and ΔC_p are evaluated for the reaction $M^{2+} + A^{2-} \rightleftharpoons MA$, and these are discussed.

Of the transition-metal dicarboxylates, the ion-pairs formed with the succinate ion involve the much less stable seven-membered ring. The smaller difference between the dissociation constants of succinic acid than between those of oxalic [2] or malonic acid [1] increases the concentration of HA^- ions, and ion-pairs such as MHA^+ have to be taken into account as well as MA when considering cells such as H_2, Pt|H_2A, NaOH, MCl_2|AgCl/Ag.

Experimental

"AnalaR" salts were used where available. Sodium perchlorate solutions were prepared from the recrystallised material and analysed by using an Amberlite IR-120 ion-exchange resin (H^+ form).

pH measurements at constant ionic strength, both in the acid buffer and in the presence of manganese ions, were made with a glass electrode in a cell of the type

Ag/AgCl, HCl|glass|solution under study|sat. KCl|calomel electrode

Glass electrodes were either commercial screened electrodes (E.I.L. type GG33), or were made from Corning 015 glass. The cell, incorporating Dunsmore and Speakman's [3] reproducible liquid junction, was maintained at 25° in an oil-bath even when not in use to prevent fluctuating calomel electrode potentials. E.M.F. measurements were made with a Tinsley potentiometer and Vibron electrometer (E.I.L. model 33B) as a null indicator; readings were reproducible to ±0·1 mv. Electrode systems were standardised with 0·01M-hydrochloric acid + 0·09M-potassium chloride which has a pH of 2·078,[4] and with 0·05M-potassium hydrogen phthalate (pH = 4·005 [5]); $[H^+]$ was obtained from pH (= $-\log a_{H^+}$) by using the mean activity data for hydrochloric acid given by Robinson and Stokes.[6] The procedure consisted in determining the pH of solutions containing known concentrations of succinic acid, sodium hydroxide, and manganese chloride, with sufficient sodium perchlorate to maintain an ionic strength of 0·2M.

For e.m.f. measurements with the cell

(1) H_2, Pt|$H_2A(m_1)$, $NaOH(m_2)$, $MCl_2(m_3)$|AgCl/Ag

The apparatus, standardisation of electrodes, and experimental technique have been described previously.[7]

Results and Discussion

E.m.f.s of cells (1) could not be interpreted in terms of only one complex MA and, in order to identify the other species present, pH measurements were made in solutions of constant ionic strength 0·2M.

It was first necessary to obtain the dissociation constants, $k_1^1 = [H^+][HA^-]/[H_2A]$ and

[1] Part VIII, *J.*, 1961, 4367.
[2] McAuley and Nancollas, *J.*, 1961, 2215.
[3] Dunsmore and Speakman, *Trans. Faraday Soc.*, 1954, **50**, 236.
[4] Hitchcock and Taylor, *J. Amer. Chem. Soc.*, 1938, **60**, 2710.
[5] British Standard, 1647, 1950.
[6] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1955.
[7] Nair and Nancollas, *J.*, 1958, 4144.

$k_2^1 = [H^+][A^{2-}]/[HA^-]$, of succinic acid at this ionic strength, and pH measurements were made in mixtures of succinic acid, sodium hydroxide, and sodium perchlorate. A graphical solution similar to that described by Speakman [8] was applied, leading to an equation $X = k_1^1 Y + k_1^1 k_2^1$, where

$$X = [H^+]^2\{[HA^-] + 2[A^{2-}]\}/\{2[H_2A] + [HA^-]\}$$

and

$$Y = [H^+]\{[H_2A] - [A^{2-}]\}/\{2[H_2A] + [HA^-]\}.$$

The results are summarised in Table 1 and X is plotted against Y in Fig. 1; the slope and intercept give $k_1^1 = 1{\cdot}38 \times 10^{-4}$ and $k_2^1 = 6{\cdot}9 \times 10^{-6}$.

In the concentration ranges used in this work, the complex species expected in solutions containing metal chloride, succinic acid, and sodium hydroxide are MA and MHA^+. A comprehensive treatment at low concentration would involve equations for total metal-ion concentration $m_3 = [M^{2+}] + [MHA^+] + [MA]$, for total succinic acid concentration $m_1 = [H_2A] + [HA^-] + [A^{2-}] + [MA] + [MHA^+]$, for electroneutrality $m_2 + [H^+] + 2[M^{2+}] + [MHA^+] = [HA^-] + 2[A^{2-}] + 2m_3$, and for the thermodynamic dissociation constants of succinic acid $k_1 = [H^+][HA^-]\gamma_1^2/[H_2A]$ and $k_2 = [H^+][A^{2-}]\gamma_2/[HA^-]$. The required association constants are $K = [MA]/[M^{2+}][A^{2-}]\gamma_2^2$, $K_1 = [MHA^+]/[M^{2+}][HA^-]\gamma_2$, and $I = 3m_3 - m_1 + 4[A^{2-}] + [H_2A] + 2[HA^-]$.

TABLE 1.

Dissociation constants of succinic acid at 25°, I = 0·2M.

10^3T_A *	10^3[Na$^+$]	10^4[H$^+$]	10^4X	10^3Y	10^3T_A *	10^3[Na$^+$]	10^4[H$^+$]	10^4X	10^3Y
7·099	2·192	2·647	1·05	1·47	7·099	3·245	1·602	0·55	0·81
7·099	2·543	2·271	0·86	1·25	12·660	7·084	1·156	0·35	0·53
7·099	2·456	2·295	0·88	1·23	12·660	14·722	0·181	−0·036	0·045
7·099	2·731	2·064	0·76	1·11	12·660	20·543	0·0437	−0·072	0·008

* T_A = Total succinic acid concentration.

At constant ionic strength, activity coefficients are omitted and the corresponding stability constants are written K^1 and K_1^1. pH measurements were made with manganese succinate over a range of concentration of metal ion and are summarised in Table 2.

TABLE 2.

Manganese succinate at 25°, I = 0·2M (K_1^1 = 5 l. mole^{-1}).

10^4[H$^+$]	10^3m_3	10^3m_1	10^3[Na$^+$]	10^3[HA$^-$]	10^3[A^{2-}]	10^3[MA]	10^3[MHA$^+$]	K_1^1	K^1
1·308	18·310	12·660	7·084	5·711	0·330	0·154	0·536	5·3	26·5
0·2079	7·324	12·660	14·772	7·744	2·809	0·552	0·277	5·5	30·3
0·2414	18·310	12·660	14·772	7·215	2·254	1·214	0·595	5·0	32·6
0·2740	36·620	12·660	14·772	6·566	1·807	1·710	1·149	5·2	28·0
0·0566	18·310	12·660	20·543	4·076	5·430	2·642	0·329	5·3	31·7
0·06528	36·620	12·660	20·790	3·562	4·114	4·208	0·591	5·2	32·1

Mean K_1^1 = 5·1. Mean K^1 = 30·1.

Various values of K_1^1 were inserted and a constant K^1 was obtained over a 23-fold variation in [H$^+$] with K_1^1 = 5 l. mole^{-1} at I = 0·2M. This provides confirmatory evidence that the second complex present in these solutions is MHA^+.

Precise e.m.f. measurements at low concentrations were then made at each temperature and K was calculated, by means of a DEUCE electronic computer, for various values of K_1 by successive approximations of I with the activity coefficient expression [9] $-\log \gamma_z = Az^2[I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) - 0{\cdot}2I]$ and the thermodynamic dissociation constants of succinic acid determined by Pinching and Bates.[10] K values at each chosen K_1 between 0 and 40 l.

[8] Speakman, *J.*, 1940, 855.
[9] Davies, *J.*, 1938, 2093.
[10] Pinching and Bates, *J. Res. nat. Bur. Stand.*, 1950, **45**, 322, 444.

mole^{-1} are given in Table 3. The mean deviation in K passes through a minimum and the corresponding K_1 was taken as the correct value; for Ni^{2+}, $K_1 = 20$; for Mn^{2+}, $K_1 = 15$; and for Co^{2+}, $K_1 = 0$. Calculation showed that these were also the best values at

TABLE 3.

Association constants at 25°.

	Nickel		Cobalt		Manganese	
K_1	$10^{-2}K$	Dev. in K (%)	$10^{-2}K$	Dev. in K (%)	$10^{-2}K$	Dev. in K (%)
0	2·13	12·5	1·65 *	3·6	1·79	15·6
2	—	—	1·67	4·5	—	—
5	2·15	9·6	1·72	5·4	1·80	10·0
10	2·17	6·6	1·79	6·6	1·82	4·7
15	2·19	3·9	1·85	8·8	1·84 *	2·2
20	2·21 *	2·3	1·92	10·5	1·86	5·5
25	2·23	2·7	1·99	12·1	1·87	10·8
30	2·25	5·3	—	—	—	—
40	2·29	10·4	—	—	—	—

* K and K_1 values adopted at 25°.

the other temperatures. The cobalt experiments were designed to limit the effect of MHA^+ and it is seen that a zero concentration of this species gives the best constancy of K. By using the appropriate K_1 values, K was evaluated at each temperature and

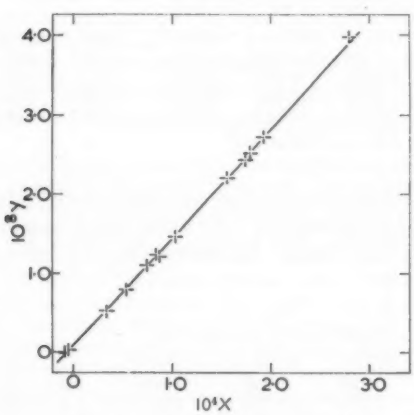


FIG. 1. Plots of X against Y.

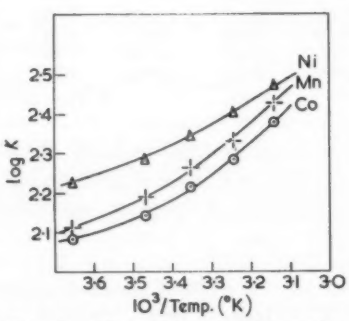


FIG. 2. Plots of log K against T^{-1}.

Table 4 shows the very good constancy obtained. The values at 25° may be compared with those given by Davies;[11] $K(CoA) = 2{\cdot}7 \times 10^2$, $K(NiA) = 2{\cdot}46 \times 10^2$, and $K(MnA) = 1{\cdot}78 \times 10^2$. The agreement is very good except in the case of cobalt.

By using γ_1 and γ_2 at $I = 0{\cdot}2$ estimated from the activity coefficient expression, K^1 values for manganese succinate, reduced to $I \longrightarrow 0$, become $K = 200$ and $K_1 = 13$, in excellent agreement with 184 and 15, respectively, in Tables 3 and 4.

Plots of log K against T^{-1} in Fig. 2 show marked curvature and may be expressed, with an accuracy of 3% in K, by the equation $\log K = a + bT + cT^2$. Values of the parameters, evaluated as described previously,[2] are given in Table 5. ΔG, ΔH, ΔC_p, and ΔS calculated from the equations $\Delta G = -\boldsymbol{R}T \ln K$, $\Delta H = 2{\cdot}303\boldsymbol{R}T^2(b + 2cT)$, $\Delta C_p = 4{\cdot}606\boldsymbol{R}T(b + 3cT)$, and $\Delta S = (\Delta H - \Delta G)/T$, are given in Table 6. ΔC_p is again seen to be subject to the greatest uncertainty. $-\Delta G$ is considerably smaller than for the

[11] Davies, *Discuss. Faraday Soc.*, 1957, **24**, 83.

TABLE 4.

Nickel succinate ($K_1 = 20$ l. mole^{-1}).

Expt.	1	2	3	4	5	6	7	8
10^3m_1 ...	2·64432	2·89030	2·61753	2·86422	5·21511	6·24147	9·15003	11·7692
10^3m_2 ...	3·48105	4·24597	2·22955	3·20346	7·99195	6·25450	8·58724	9·92814
10^3m_3 ...	3·97073	3·95576	5·08036	4·26079	7·24212	4·26849	5·61057	10·62220

Expt.	$E^1 - E^\circ$	10^6[H$^+$]	10^2I	10^3[HA$^-$]	10^4[A^{2-}]	10^3[M^{2+}]	10^4[MA]	$10^{-2}K$
				At 0°				
1	0·40142	6·361	1·548	1·458	7·863	3·712	1·954	1·76
2	0·41305	3·874	1·642	1·319	11·824	3·643	2·539	1·59
6	0·37687	16·960	1·899	4·014	8·482	3·896	1·855	1·64
7	0·36519	21·889	2·503	5·759	10·055	5·031	2·591	1·67
8	0·34184	33·181	4·038	6·832	8·913	9·628	3·519	1·71
							Mean	1·67 ± 0·05
				At 15°				
3	0·37908	29·899	1·732	1·616	2·072	4·918	0·674	1·87
4	0·40359	13·155	1·589	1·799	5·146	4·022	1·507	1·98
5	0·42051	4·211	2·938	2·080	21·512	6·366	7·376	1·96
6	0·39479	19·079	1·893	4·032	8·267	3·883	2·030	1·86
7	0·38238	24·730	2·495	5·782	9·767	5·014	2·798	1·91
8	0·35768	37·645	4·031	6·859	8·649	9·617	3·716	1·93
							Mean	1·92 ± 0·04
		10^5[H$^+$]						
				At 25°				
1	0·43442	0·737	1·538	1·648	0·758	3·689	2·202	2·15
3	0·39088	3·157	1·729	1·617	1·999	4·912	0·752	2·20
4	0·41660	1·373	1·585	1·805	5·030	4·014	1·595	2·18
5	0·43388	0·444	2·910	2·083	20·800	6·297	8·085	2·28
6	0·40734	2·004	1·885	4·043	8·028	3·865	2·226	2·15
7	0·39441	2·608	2·484	5·794	9·447	4·989	3·088	2·24
8	0·36873	3·994	4·019	6·861	8·322	9·589	4·087	2·27
							Mean	2·21 ± 0·05
				At 35°				
1	0·44860	0·751	1·530	1·472	7·366	3·670	2·395	2·46
3	0·40334	3·260	1·726	1·621	1·919	4·905	0·821	2·55
4	0·43000	1·408	1·579	1·811	4·863	4·001	1·737	2·51
5	0·44801	0·453	2·888	2·088	20·221	6·243	8·649	2·59
6	0·42043	2·056	1·877	4·060	7·767	3·848	2·413	2·46
7	0·40698	2·685	2·474	5·816	9·117	4·969	3·324	2·56
8	0·38029	4·141	4·008	6·877	7·982	9·565	4·397	2·62
							Mean	2·53 ± 0·05
				At 45°				
1	0·46313	0·749	1·522	1·478	7·134	3·650	2·603	2·82
3	0·41617	3·304	1·723	1·625	1·830	4·899	0·895	2·98
4	0·44374	1·426	1·571	1·814	4·633	3·980	1·956	3·03
5	0·46249	0·456	2·856	2·093	19·389	6·164	9·471	3·05
6	0·43403	2·069	1·868	4·078	7·469	3·828	2·632	2·85
7	0·42011	2·708	2·464	5·842	8·761	4·947	3·569	2·93
8	0·39235	4·212	3·996	6·892	7·608	9·540	4·737	3·04
							Mean	2·96 ± 0·08

Cobalt succinate ($K_1 = 0$)

Expt.	1	2	3	4	5	6
10^3m_1	4·5096	5·0085	3·6668	3·7054	3·8596	3·7091
10^3m_2	4·5314	4·8902	5·1766	5·1137	5·0583	4·7523
10^3m_3	6·5698	7·0268	5·4807	5·8234	5·9076	5·5273

Expt.	$E^1 - E^\circ$	10^5[H$^+$]	10^2I	10^3[HA$^-$]	10^3[A^{2-}]	10^4[MA]	$10^{-2}K$
				At 0°			
1	0·36658	1·757	2·446	2·971	0·643	1·465	1·15
2	0·36272	1·952	2·615	3·282	0·650	1·640	1·23
3	0·39994	0·505	2·219	1·877	1·381	2·711	1·16
4	0·39579	0·569	2·304	1·968	1·296	2·803	1·23
5	0·39025	0·710	2·314	2·202	1·163	2·688	1·29
6	0·39012	0·757	2·172	2·178	1·063	2·285	1·24
						Mean	1·24 ± 0·04

TABLE 4. (*Continued.*)

Expt.	$E^1 - E'$	$10^5[H^+]$	10^2I	$10^3[HA^-]$	$10^3[A^{2-}]$	$10^4[MA]$	$10^{-2}K$
			At 15°				
3	0·41944	0·561	2·212	1·883	1·362	2·880	1·29
4	0·41502	0·634	2·297	1·974	1·276	2·977	1·36
5	0·40924	0·789	2·310	2·211	1·149	2·782	1·39
6	0·40877	0·852	2·161	2·182	1·033	2·562	1·47
						Mean	1·37 ± 0·05
			At 25°				
1	0·39599	2·089	2·433	2·986	0·605	1·787	1·56
2	0·39183	2·316	2·603	3·302	0·614	1·918	1·60
3	0·43279	0·590	2·194	1·884	1·316	3·331	1·58
4	0·42809	0·670	2·278	1·974	1·226	3·472	1·69
5	0·42203	0·837	2·291	2·210	1·101	3·274	1·75
6	0·42192	0·891	2·151	2·187	1·007	2·799	1·69
						Mean	1·65 ± 0·06
			At 35°				
1	0·40864	2·150	2·426	2·995	0·584	1·954	1·81
2	0·40426	2·391	2·595	3·310	0·590	2·121	1·88
3	0·44678	0·604	2·177	1·887	1·273	3·752	1·89
4	0·44201	0·684	2·264	1·978	1·191	3·806	1·96
5	0·43564	0·858	2·277	2·215	1·064	3·616	2·05
6	0·43547	0·916	2·137	2·191	0·972	3·140	2·01
						Mean	1·93 ± 0·07
			At 45°				
1	0·42137	2·202	2·411	2·990	0·548	2·338	2·37
2	0·41700	2·436	2·582	3·310	2·559	2·437	2·35
3	0·46114	0·610	2·154	1·889	1·215	4·321	2·34
4	0·45608	0·694	2·240	1·979	1·130	4·405	2·45
5	0·44959	0·868	2·257	2·217	1·015	4·102	2·50
6	0·44945	0·925	2·120	2·194	0·928	3·562	2·45
						Mean	2·41 ± 0·06

Manganese succinate ($K_1 = 15$)

Expt.	1	2	3	4	5	6	7	8
10^3m_1 ...	3·87732	3·58060	4·10579	3·73456	3·84355	3·70642	7·12848	8·07886
10^3m_2 ...	2·72403	3·64612	3·40891	3·65978	4·42001	4·20629	8·56922	9·41907
10^3m_3 ...	4·89358	5·65596	4·90255	3·54878	9·83515	8·44751	10·28948	9·68893

Expt.	$E^1 - E^\circ$	$10^5[H^+]$	10^2I	$10^3[HA^-]$	$10^4[A^{2-}]$	$10^3[M^{2+}]$	$10^4[MA]$	$10^{-2}K$
				At 0°				
1	0·35267	4·096	1·731	2·201	1·888	4·753	0·458	1·41
2	0·37151	1·620	2·060	2·290	5·182	5·438	1·092	1·16
3	0·36168	2·822	1·802	2·537	3·186	4·718	0·777	1·45
5	0·36559	1·274	3·359	2·285	7·386	9·417	2·523	1·38
7	0·36851	1·098	3·915	4·151	16·220	9·550	4·460	1·19
8	0·36778	1·200	3·832	4·833	17·188	8·948	4·194	1·11
							Mean	1·28 ± 0·13
				At 15°				
1	0·36921	4·617	1·730	2·213	1·838	4·752	0·476	1·54
5	0·38291	1·437	3·353	2·293	7·201	9·403	2·686	1·55
6	0·38621	1·436	2·927	2·253	6·825	8·075	2·297	1·52
7	0·38543	1·264	3·882	4·148	15·407	9·470	5·332	1·55
8	0·38453	1·388	3·791	4·822	16·211	8·848	5·278	1·54
							Mean	1·54 ± 0·02
				At 25°				
1	0·38077	4·869	1·729	2·218	1·777	4·747	0·532	1·81
5	0·39468	1·531	3·340	2·292	6·884	9·371	3·029	1·88
6	0·39818	1·527	2·916	2·252	6·539	8·046	2·602	1·83
7	0·39730	1·348	3·854	4·145	14·718	9·402	6·065	1·90
8	0·39666	1·463	3·773	4·832	15·708	8·804	5·759	1·78
							Mean	1·84 ± 0·04
				At 35°				
3	0·40296	3·435	1·795	2·570	2·913	4·705	0·926	2·01
4	0·42438	2·066	1·424	2·471	4·422	3·349	1·246	2·26
5	0·40702	1·592	3·327	2·293	6·566	9·341	3·356	2·23
6	0·41074	1·581	2·905	2·255	6·264	8·021	2·872	2·16
7	0·41010	1·383	3·839	4·161	14·286	9·368	6·434	2·13
8	0·40925	1·511	3·751	4·843	15·109	8·752	6·326	2·09
							Mean	2·15 ± 0·07

TABLE 4. (*Continued.*)

Expt.	E^1-E°	$10^5[H^+]$	10^2I	$10^3[HA^-]$	$10^4[A^{2-}]$	$10^3[M^{2+}]$	$10^4[MA]$	$10^{-2}K$
				At 45°				
4	0·43792	2·093	1·417	2·476	4·211	3·330	1·439	2·80
5	0·41962	1·637	3·310	2·289	6·154	9·299	3·800	2·78
6	0·42334	1·633	2·887	2·249	5·836	7·976	3·347	2·78
7	0·42309	1·407	3·812	4·167	13·572	9·302	7·147	2·57
8	0·42212	1·543	3·719	4·846	14·298	8·675	7·154	2·58
							Mean	2·70 ± 0·10

TABLE 5.

Parameters for temperature-dependence of log K.

	a	-10^2b	10^5c
NiA	3·560	1·384	3·274
CoA	6·041	3·255	6·615
MnA	4·006	1·912	4·453

corresponding malonate complexes [1] owing to the lower stability of the seven-membered ring.

$\Delta S_{hyd}(MA)$ may be written:

$$\Delta S_{hyd}(MA) = \Delta S - \Delta S_g + \Delta S_{hyd}(M^{2+}) + \Delta S_{hyd}(A^{2-})$$

where ΔS_{hyd} and ΔS_g are hydration and gaseous entropies respectively. ΔS_g has been calculated as described previously,[12] a planar model being used for the complex species.

TABLE 6.

Thermodynamic properties.

Reaction	ΔH (kcal. mole^{-1})	ΔG (kcal. mole^{-1})	ΔS (cal. deg.$^{-1}$ mole^{-1})	ΔC_p (cal. deg.$^{-1}$)
$Ni^{2+} + A^{2-}$	2·23 ± 0·2	−3·20 ± 0·02	18·2 ± 0·7	42 ± 20
$Co^{2+} + A^{2-}$	2·81 ± 0·04	−3·02 ± 0·02	19·6 ± 0·1	72 ± 20
$Mn^{2+} + A^{2-}$	2·95 ± 0·1	−3·09 ± 0·02	20·3 ± 0·2	62 ± 15

TABLE 7.

Entropies (in cal. deg.$^{-1}$ mole^{-1}).

Ion pair	$S_g(MA)$	ΔS	$S^\circ(MA)$	$-\Delta S_{hyd}(MA)$	r_+^{-1} (Å^{-1})
NiA	70·6	18·2	+1·1	69·5	1·37
CoA	70·6	19·6	+3·5	67·1	1·35
MnA	70·5	20·3	+6·2	64·4	1·28

$\Delta S_{hyd}(A^{2-})$ was interpolated on a plot of ΔS_{hyd} of a number of bivalent anions against r_-^{-1}, r_- having been calculated from the corresponding ionic mobilities.[13] Entropies are summarised in Table 7. $\Delta S_{hyd}(MA)$ follow the order oxalate > malonate > succinate and may reflect an increasing polarity of the complexes accompanying reduced stability. The importance of using hydration entropies, and not entropies of association for correlation with r_+^{-1}, is seen in Table 7; the two terms vary in opposite directions.

Heats of formation vary in the same sense as for the oxalates and malonates, in the reverse order to changes in ionisation potential I_{02}.

We thank the D.S.I.R. for a grant to A. McA., and Dr. V. S. K. Nair for assistance with some of the experimental work.

CHEMISTRY DEPARTMENT, THE UNIVERSITY, GLASGOW, W.2. [*Received, April 13th*, 1961.]

[12] Nair and Nancollas, *J.*, 1958, 3706.
[13] Jenkins and Monk, *J.*, 1951, 68.

879. *β-Glucopyranosides of Hydroxymethyl- and Hydroxyethylferrocene.*

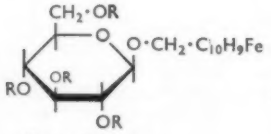
By A. N. de Belder, E. J. Bourne, and J. B. Pridham.

Synthesis and properties of ferrocenylmethyl and ferrocenylethyl β-D-glucopyranoside are described. The sensitivites of the compounds to dilute mineral acid have been investigated.

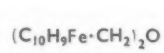
As a first step in the study of carbohydrate derivatives of ferrocene, ferrocenylmethyl β-D-glucopyranoside (Ia) has been prepared by the Koenigs–Knorr [1] reaction under the conditions recommended by Reynolds and Evans.[2]

Condensation of hydroxymethylferrocene with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in the presence of silver oxide and calcium sulphate yielded mainly ferrocenylmethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (Ib), with some di(ferrocenylmethyl) ether (II). Deacetylation gave yellow crystals of the glucoside (Ia) monohydrate. This was also prepared in low yield by reaction of D-glucose with hydroxymethylferrocene in the presence of toluene-*p*-sulphonic acid.[3]

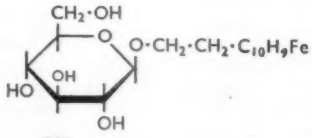
The structure of the glucoside (Ia) was proved by acidic and enzymic hydrolyses, methylation, and periodate oxidation. Potassium metaperiodate, in addition to reacting with the glucosyl residue, degraded the ferrocene nucleus, producing insoluble material which was probably a mixture of ferric hydroxide and ferric periodate or possibly potassium periodate adsorbed on ferric hydroxide. Ferric salts interfered with the periodate consumption (cf. Lang and Faude [4]), so the acetate (Ib) and the glucoside (Ia)



(I) a: R = H
b: R = Ac



(II)



(III)

were oxidised in identical conditions and the periodate uptake by the glucosyl residue of (Ia) and the formaldehyde liberation were calculated by difference. In this way it was shown that the glucosyl group consumed 2 mol. of oxidant and produced no formaldehyde, consistently with a glucopyranoside structure. Methylation of the glucoside, followed by hydrolysis, yielded crystalline 2,3,4,6-tetra-*O*-methyl-D-glucose. Emulsin hydrolysed the glucoside to glucose and hydroxymethylferrocene, and this result together with the specific optical rotation of the compound ($[\alpha]_D^{22}$ −37·7°) confirms the view that the molecule is a β-glucopyranoside.

Table 1.

Hydrolysis of the glucoside (Ia; 0·0218M) in 0·048N-H_2SO_4.

Time (min.) ...	0	8	15	21	26	∞
α_D^{25}	−0·28° (calc.)	−0·04°	+0·05°	+0·11°	+0·13°	+0·18° (calc.)
k_1 (min.$^{-1}$)	—	0·088	0·083	0·088	0·084	—

0·048N-Sulphuric acid rapidly hydrolysed the glucoside at 25°, giving hydroxymethylferrocene, glucose, and di(ferrocenylmethyl) ether (II). The first-order rate constant for this reaction was 8·6 × 10^{-2} min.$^{-1}$ (Table 1), which resembles the value for the hydrolysis

[1] Koenigs and Knorr, *Ber.*, 1901, **34**, 957.
[2] Reynolds and Evans, *J. Amer. Chem. Soc.*, 1938, **60**, 2559.
[3] Combs, McCloskey, Sundberg, and Coleman, *J. Amer. Chem. Soc.*, 1949, **71**, 276.
[4] Lang and Faude, *Z. anorg. Chem.*, 1937, **232**, 271.

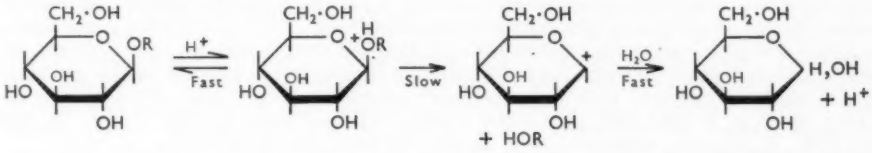
of a furanoside rather than a pyranoside.[5] The nature of the bond fission was therefore investigated by conducting the hydrolysis in the presence of $H_2{}^{18}O$. This indicated that the hydrolysis occurred predominantly by hexosyl–oxygen bond fission (Table 2). Similar results have been obtained by Bunton *et al.*[6,7] with methyl and phenyl glucopyranosides, methyl 2-deoxyglucopyranosides, and maltose. No conclusions can be drawn from the isotope experiments regarding the formation of the ether: it could be formed by direct reaction of a ferrocenylmethyl cation with the glucoside (Ia) or by further reaction of the hydroxymethylferrocene liberated in the hydrolysis.

TABLE 2.

	Fcn·CH_2·OH	Fcn·CH_2·O·CH_2·Fcn	Glucose *	Fcn·CH_2·OH (control)	Glucose (control)	Water
Abundance (atom %) †	0·35	0·25	0·93	0·18 ‡	0·18	1·11
Excess abundance (atom %) ...	0·17	0·07	0·74	0	0	0·93

* Calculated from the observed isotopic ratio on the assumption that only the 1-hydroxyl group was enriched. † ^{18}O atom % abundance is given by $100 - (2R + 1)$ when R is $[C^{16}O_2]/[C^{18}O^{16}O]$. ‡ Normal abundance.

Bunton *et al.*[6,7] have shown that the acidic hydrolysis of a number of glucopyranosides proceeds by the annexed mechanism. The alternative scheme whereby the cyclic oxygen atom is protonated and the carbonium ion is formed by ring-opening between $C_{(1)}$ and this oxygen atom is not favoured.



The rates of hydrolysis of some glucosides[8] increase as the aglycone residue is changed from a primary to a tertiary group. In some respects hydroxymethylferrocene has properties characteristic of a tertiary alcohol. For example, it is readily converted into an ether (II) in the presence of acid[9] and attempts to prepare its toluene-*p*-sulphonate in pyridine produce the 1-ferrocenylmethylpyridinium salt.[10] Bunton *et al.*[7] have recently shown that t-butyl D-glucopyranoside is rapidly hydrolysed by acid, but in this instance by alkyl–oxygen bond fission and not by the hexosyl–oxygen bond fission which occurs predominantly with ferrocenylmethyl β-D-glucopyranoside. Ferrocene has many properties characteristic of a highly activated benzene derivative,[11] so in the case of the glucoside (Ia) the ferrocene nucleus might be expected to increase the basicity of the exocyclic oxygen atom and thereby facilitate formation of the conjugate acid during hydrolysis. Nath and Rydon[12] showed that the introduction of electron-repelling groups into the aromatic ring of phenyl β-D-glucopyranoside increased the lability of this glucoside to acid, but comparatively slightly. Edward[13] suggested that phenyl glucosides are under strain. Thus the resulting lack of planarity may restrict the conjugate displacements in these molecules and the polar influences would then be small. A model of the glucoside (Ia) shows that there is no marked intramolecular steric pressure, and polar

[5] Pigman and Goepp. "Chemistry of the Carbohydrates," Academic Press Inc., New York, 1948, p. 206.
[6] Bunton, Lewis, Llewellyn, and Vernon, *J.*, 1955, 4419.
[7] Armour, Bunton, Patai, Selman, and Vernon, *J.*, 1961, 412.
[8] Veibel and Hjorth, *Acta Chem. Scand.*, 1952, **6**, 1353.
[9] Hauser and Cain, *J. Org. Chem.*, 1958, **23**, 2007.
[10] de Belder, Bourne, and Pridham, unpublished results.
[11] Pauson, "Non-Benzenoid Aromatic Compounds," Interscience Publ., Inc., New York, 1959, p. 123.
[12] Nath and Rydon, *Biochem. J.*, 1954, **57**, 1.
[13] Edward, *Chem. and Ind.*, 1955, 1102.

influences therefore presumably play the more important rôle in the stability of this compound to acid.

Ferrocenylethyl β-D-glucopyranoside, also prepared by the Koenigs–Knorr method, was virtually stable to 0·05N-sulphuric acid at 25° and was incompletely hydrolysed by this acid after 20 hr. at 70°. The greater stability of this glucoside (II) than of ferrocenylmethyl β-D-glucopyranoside (Ia) is presumably due to the additional carbon atom in the former which reduces the electrical influence of the ferrocene nucleus.

Further quantitative studies of the substitution of ferrocene and its derivatives may clarify the position and it is obvious that great care must be taken in assigning pyranoside or furanoside structures solely on the basis of stability to acid.

Experimental

Butan-1-ol–ethanol–water (4 : 1 : 5, v/v; organic layer) was used for the paper chromatography of sugars, and a system comprising two organic phases [14] for ferrocene derivatives.

Hydroxymethylferrocene.—This compound was prepared from (ferrocenylmethyl)trimethylammonium iodide,[15] as described by Hauser and Lindsay,[16] and, recrystallised from hexane, had m. p. 75—76° (lit.,[17] 76°).

Hydroxyethylferrocene.—Acetylferrocene was converted into this compound as described by Rinehart, Curby, and Sokol; [18] the product had m. p. 45—47° (lit.,[18] 49—50°) after recrystallisation from ether–hexane.

Ferrocenylmethyl 2,3,4,6-Tetra-O-acetyl-β-D-glucopyranoside (Ib) (*Köenigs–Knorr Method*).—2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (4·1 g.) in methylene chloride (30 ml.) was added slowly to a mixture of hydroxymethylferrocene (3·3 g.), silver oxide (9·2 g.), and calcium sulphate (5·0 g.) in methylene chloride (30 ml.), that was then shaken for 18 hr., filtered, and evaporated to dryness. The residue dissolved in hot methanol and on cooling gave a precipitate which when recrystalliised from benzene–hexane afforded orange crystals of the *acetate* (Ib) (3·0 g., 54%), m. p. 183—185°, $[\alpha]_D^{21}$ −11·7° (*c* 1·0 in $CHCl_3$) (Found: C, 55·0; H, 5·8; Fe, 10·0; Ac, 31·3. $C_{25}H_{30}FeO_{10}$ requires C, 54·9; H, 5·7; Fe, 10·2; Ac, 31·5%).

Di(ferrocenylmethyl) Ether (II).—Fractionation of the methanolic filtrate from the Koenigs–Knorr reaction [remaining after the precipitation of the acetate (Ib)] on a column of alumina (with benzene, benzene–hexane, and benzene–chloroform) produced crystals of di(ferrocenylmethyl) ether (0·9 g.), m. p. 130—131° (lit.,[19] 129—130°) (Found: C, 63·3; H, 5·5. Calc. for $C_{22}H_{22}OFe_2$: C, 63·8; H, 5·4%).

Ferrocenylmethyl β-D-Glucopyranoside (Ia).—The acetate (Ib) (1·0 g.) was treated with 0·2N-sodium methoxide (1 ml.) in methanol–chloroform at room temperature for 24 hr. The resulting water-soluble fraction contained the *glucoside* (Ia) which after one recrystallisation from water was obtained as yellow plates of the monohydrate (0·4 g., 50%), m. p. 135—136°, $[\alpha]_D^{22}$ −37·7° (*c* 1·0 in H_2O) (Found: C, 51·8; H, 6·3; Fe, 14·1%; H_2O, 0·98 mol. $C_{17}H_{22}FeO_6,H_2O$ requires C, 51·5; H, 6·1; Fe, 14·1%).

Ferrocenylmethyl β-D-Glucopyranoside (Ia) (*Fischer Method*).—Hydroxymethylferrocene (0·1 g.), D-glucose (0·05 g.), and toluene-*p*-sulphonic acid (5 mg.) in dimethylformamide (5 ml.) were heated for 6 hr. at 80—90°. Fractionation of the mixture by partition chromatography on Whatman No. 3MM paper yielded a small specimen of the glucoside (Ia), m. p. 133—136°.

Hydrolysis of the Glucoside (Ia).—(a) *With Amberlite* IR-120 (H^+ *form*) *resin.* The glucoside (50 mg.) in 90% aqueous ethanol was shaken with the resin for 2 hr. at 80—90°. The resulting glucose and hydroxymethylferrocene were identified by paper chromatography.

(b) *With emulsin.* The glucoside (5 mg.) was incubated with emulsin solution (3 ml.) at 30° for 18 hr., and the products, glucose and hydroxymethylferrocene, were characterised by paper chromatography.

Methylation of the Glucoside (Ia).—Silver oxide (0·5 g.) was added during 30 min., with continual agitation, to the glucoside (0·2 g.) in dimethylformamide (5 ml.) and methyl iodide (1 ml.). Shaking was continued for 18 hr. and the product isolated by partition between water

[14] de Belder, Bourne, and Pridham, *Chem. and Ind.*, 1959, 996.
[15] Osgerby and Pauson, *J.*, 1958, 656.
[16] Hauser and Lindsay, *J. Org. Chem.*, 1956, **21**, 382.
[17] Broadhead, Osgerby, and Pauson, *J.*, 1958, 650.
[18] Rinehart, Curby, and Sokol, *J. Amer. Chem. Soc.*, 1957, **79**, 3420.
[19] Graham, Lindsey, Parshall, Peterson, and Whitman, *J. Amer. Chem. Soc.*, 1957, **79**, 3416.

XUM

and chloroform. The methylation was repeated and the product isolated as a syrup (0·1 g.) that was dissolved in N-hydrochloric acid (10 ml.); steam was passed through this solution for 30 min. After cooling, hydroxymethylferrocene was removed by extraction with ether. The hydrolysate was then saturated with sodium sulphate and extracted with chloroform. The chloroform solution was decolorised with charcoal, dried ($MgSO_4$), and concentrated to a syrup. 2,3,4,6-Tetra-*O*-methyl-D-glucose (40 mg.), m. p. 96—97°, mixed m. p. 95—97°, was obtained from a light petroleum (b. p. 40—60°) solution of this, and its identity was confirmed by paper chromatography.

Periodate Oxidations.—The glucoside (Ia) (10—20 mg.) was dissolved in dioxan (20 ml.), and 0·02M-potassium metaperiodate (30 ml.; adjusted to pH 7) was added. Samples (3 ml.) were removed at intervals and the periodate uptake and formaldehyde liberation determined by the methods of Fleury and Lange [20] and O'Dea and Gibbons,[21] respectively. The experiment was repeated with the acetate (Ib).

Time (hr.)		5	8	10
Periodate consumed (mol.) :	acetate (Ib)	10·5	11·5	11·5
	glucoside (Ia)	12·0	13·5	13·5

Kinetic Measurements.—The acidic hydrolysis at 25° was followed by dissolving the glucoside (Ia) in water (25 ml.), then adding N-sulphuric acid (1·25 ml.). At intervals samples (5 ml.) were withdrawn, neutralised with 0·05N-ammonia, and centrifuged and the optical rotations of the solutions were then measured. The hydrolysis was carried out with the glucoside at 0·0218M-concentration (Table 1). Errors between calculated and observed values by this procedure were generally less than 4%.

Hydrolysis of Glucoside (Ia) *in the Presence of* $H_2{}^{18}O$.—The glucoside (*ca.* 0·4 g.) was dissolved in ^{18}O-enriched water (30 ml.; 0·8 atom %). N-Sulphuric acid (1·5 ml.) was added. The solution was left at room temperature for 45 min., then extracted with benzene. The aqueous layer was shaken with an excess of barium carbonate, filtered, and treated with Biodeminrolit (carbonate form). After filtration and freeze-drying the resulting glucose crystallised from methanol–water–propan-2-ol (m. p. 149—152°). The benzene layer was washed with water and dried (K_2CO_3). Fractionation on an alumina column yielded hydroxymethylferrocene (40 mg.), m. p. 74—76°, and di(ferrocenylmethyl) ether (50 mg.), m. p. 130—131°.

Control experiments with β-D-glucose and hydroxymethylferrocene were carried out under the same conditions.

All compounds were analysed isotopically as carbon dioxide.[22]

Ferrocenylethyl β-D-*Glucopyranoside* (III).—Hydroxyethylferrocene (0·39 g.) in methylene chloride (3 ml.) was added to 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (0·62 g.), silver oxide (0·5 g.), and calcium sulphate (0·5 g.) in methylene chloride (5 ml.), and the mixture was shaken for 20 hr. Filtration followed by removal of the solvent left a residue which was dissolved in methanol. 0·1N-Sodium methoxide (1 ml.) was then added and the products were partitioned between water and chloroform. The aqueous layer was freeze-dried and the residual *glucoside* (0·1 g.) (III) crystallised from water; it had m. p. 174°, $[\alpha]_D^{23} - 28°$ (*c* 0·3 in H_2O) (Found: C, 55·3; H, 6·1. $C_{18}H_{24}FeO_6$ requires C, 55·1; H, 6·2%).

Hydrolysis of Glucoside (III):—(a) *With acid.* The glucoside (10 mg.) was dissolved in 0·05N-sulphuric acid (10 ml.) at 25° and samples (1 ml.) were removed at intervals, neutralised with barium carbonate, and examined for glucose on paper chromatograms. This experiment was repeated at 70°.

(b) *With emulsin.* This was carried out under the conditions described for the hydrolysis of the glucoside (Ia). The resulting glucose and hydroxyethylferrocene were identified by paper chromatography.

We are grateful to Dr. C. A. Bunton for a gift of ^{18}O-enriched water and to Drs. J. Brimacombe, A. B. Foster, and J. Majer for assistance with the isotopic analyses. One of us (A. N. de B.) is indebted to Aspro-Nicholas Ltd. for a grant.

ROYAL HOLLOWAY COLLEGE,
ENGLEFIELD GREEN, SURREY. [*Received, April 19th,* 1961.]

[20] Fleury and Lange, *J. Pharm. Chim.*, 1933, **17**, 107.
[21] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.
[22] Doering and Dorfman, *J. Amer. Chem. Soc.*, 1953, **75**, 5595.

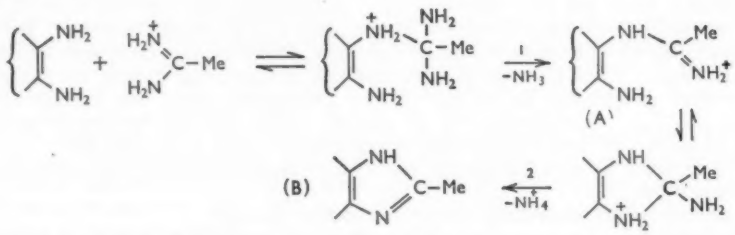
880. *The Synthesis of 8-Substituted Purines.*

By F. Bergmann and M. Tamari.

4,5-Diaminopyrimidines condense with amidine salts, giving 8-substituted purines. High yields are obtained with 4,5-diaminouracil and its mono- and di-thio-derivatives, but they are lower with 6-substituted diaminopyrimidines. 2-Hydroxy-8-methylpurine is unstable in dilute sulphuric acid, and 3,8-dimethyl-6-thioxanthine is unstable under all conditions, so that it could not be isolated.

Introduction of a methyl group into position 8 of the purine ring has been effected previously by condensation of the appropriate 4,5-diaminopyrimidines with acetic anhydride [1,2] or with a mixture of this reagent and ethyl orthoacetate.[3] A similar principle underlies the method of Richter, Loeffler, and Taylor, who condensed aminomalonamidamidine with orthoacetate.[4] These procedures require drastic conditions and the yields are often unsatisfactory.

An alternative method, in which ammonia is eliminated instead of water or alcohol, has proved in our hands to be superior in most cases. Condensation of an acetamidine salt with an appropriate derivative of 4,5-diaminopyrimidine in the absence of a solvent leads directly and in high yields to the desired 8-methylpurines. The conditions used are analogous to those applied by Galat and Elion to the amidation of esters by molten ammonium salts.[5]



A number of 8-methyl derivatives, obtained in this way, are listed in Table 1. Likewise, benzamidine gave 8-phenylpurines, which indicates that the method may be generally applicable.

The detailed mechanism of the condensation may be formulated as a series of acid-catalysed transamidations, in analogy with the mechanism of acid hydrolysis of amides [6] or of the conversion of orthoformate into formamidines.[7] The reaction illustrated takes place only between an amidine salt and a free diaminopyrimidine, but fails with the sulphates of the latter. This observation indicates that in the intermediate phases of the reaction the proton of the amidinium ion is redistributed between the various basic groups present, in order to make possible the stepwise elimination of two molecules of ammonia. In the first step, ammonia is liberated, while the proton remains on the intermediate amidine (A), which is the stronger base. In the second step, however, ammonium ion is removed, because now ammonia (pK 9·2) surpasses the basicity (pK ~2) of the imidazole ring [8,9] in (B).

[1] Isay, *Ber.*, 1906, **39**, 250.
[2] Johns, *J. Biol. Chem.*, 1912, **67**, 11.
[3] Koppel and Robins, *J. Org. Chem.*, 1958, **23**, 1457.
[4] Richter, Loeffler, and Taylor, *J. Amer. Chem. Soc.*, 1960, **82**, 3144.
[5] Galat and Elion, *J. Amer. Chem. Soc.*, 1943, **65**, 1566.
[6] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, New York, 1953, p. 786.
[7] Roberts, *J. Amer. Chem. Soc.*, 1950, **72**, 3603.
[8] Albert and Brown, *J.*, 1954, 2060.
[9] Bergmann and Dikstein, *J. Amer. Chem. Soc.*, 1955, **77**, 691.

The best yields were obtained in the condensation of 4,5-diaminouracil and its thio-derivatives. If only a 6-hydroxyl group was present condensation with acetamidine or benzamidine hydrochloride gave inferior results, but these were somewhat improved by using the amidine acetates. The latter also reacted faster than the hydrochlorides, in

TABLE 1.

(*a*) 8-Substituted purines, obtained by condensation of amidines and 4,5-diaminopyrimidines.

No.	Substituent at position 2	4	8	Reaction time (min.)	Yield (%)	$\lambda_{max.}$ (mμ) at pH 8·0	R_F in solvent [a] A	B	C	Fluorescence
1 [c]	H	OH	Me	60	56 (67) [b]	252	0·57	0·70	—	Violet
2 [c]	OH	OH	Me	30	94	240, 275	0·54	0·60	0·42	,,
3	OH	SH	Me	35	83 [d]	251, 344	0·50	0·56	0·57	Blue
4 [e]	SH	OH	Me	30	77	235, 280	0·45	0·74	0·61	Violet
5 [e]	SH	SH	Me	25	65 (86)	247, 285, 351	0·53	0·59	0·71	Blue
6	SH	NH_2	Me	30	66	230, 251, 280	0·61	0·67	—	Blue
7	H	OH	Ph	70	50 (78)	291	0·58	0·79	—	Blue
8 [e]	OH	OH	Ph	40	80	228, 309	0·52	0·66	—	Blue

No.	Found (%) C	H	N	Formula	Required (%) C	H	N
3	39·3	3·3	30·5	$C_6H_6N_4OS$	39·6	3·3	30·8
6	29·2	3·8	27·8	$C_6H_7N_5S,\frac{1}{2}H_2SO_4,H_2O$	29·0	4·0	28·2
7	62·4	3·6	26·4	$C_{11}H_8N_4O$	62·3	3·8	26·4

[a] Solvents: A, 95% EtOH–H_2O–AcOH 85 : 10 : 5 (v/v); B, 95% EtOH–pyridine–H_2O 70 : 20 : 10 (v/v); C, propan-2-ol–dimethylformamide–10% NH_3 65 : 25 : 10 (v/v). [b] Figures in parentheses are the yields obtained with acetamidine acetate. [c] Koppel and Robins, ref. 3. [d] This compound was also prepared by reaction of 8-methylxanthine with phosphorus pentasulphide in 90% yield. [e] Cook and Thomas (*J.*, 1950, 1884) obtained this purine in 20% yield by a different method. [f] Nos. 1—6 needles, 7 and 8 rods; nos. 1—5 from H_2O; no. 6 from 5% H_2SO_4; no. 7 reprecipitated; no. 8 from dil. NH_3.

(*b*) 3,8-Dimethylpurines obtained by direct condensation.

No.	2-Subst.	Yield (%)	$\lambda_{max.}$ (mμ) at pH 8·0	R_F in solvent A	B	C	Fluorescence
9	O	92	275	0·64	0·79	0·68	Blue
10	S	88	233, 288	0·60	0·84	—	Violet

No.	Form and solvent	Found (%) C	H	N	Formula	Required (%) C	H	N
9	Needles H_2O	46·2	4·5	30·6	$C_7H_8N_4O_2$	46·7	4·4	31·1
10	Prisms ,,	43·0	3·6	28·7	$C_7H_8N_4OS$	42·9	4·1	28·6

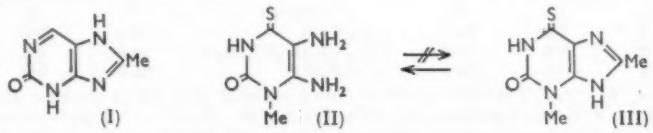
contradiction to the relative strengths of acetic and hydrochloric acid in water. A similar reversed order of catalytic activity has been reported for amidations of esters in liquid ammonia;[10,11] but the present experiments have not been extended to embrace the whole series of acids studied by previous authors.

Condensation failed with 4,5-diamino-6-mercaptopyrimidine. Therefore, 6-mercapto-8-methylpurine was prepared by thiation of the corresponding hypoxanthine (no. 1 in Table 1).

[10] Fellinger and Audrieth, *J. Amer. Chem. Soc.*, 1938, **60**, 579.
[11] Shatenshtein, *J. Amer. Chem. Soc.*, 1937, **59**, 432.

The reaction with 4,5-diamino-2-hydroxypyrimidine was attempted under a variety of conditions. The best results were achieved by condensation with acetamidine acetate at 140—145°. Even then, as shown by paper chromatography, a mixture of compound (I) and the original pyrimidine was obtained, from which pure 2-hydroxy-8-methylpurine could not be isolated. Therefore, we have used an alternative route, namely, desulphuration of the corresponding 6-thio-derivative (no. 3 in Table 1) in ammoniacal solution. Compound (I) cannot be isolated as its sulphate. Even 1% sulphuric acid in absolute ethanol at 0° opened the imidazole ring. Clearly this compound is considerably more sensitive to acids than its parent 2-hydroxypurine: >90% of the latter is decomposed in N-sulphuric acid at 100° in 1 hr.[8] It therefore appears remarkable that Johns [2] isolated compound (I) as its nitrate from a 30% solution of nitric acid: in our hands, such concentrated acid caused ring opening, whereas dilute nitric acid (pH 2) produced the crystalline nitrate after 2 months' storage at room temperature.

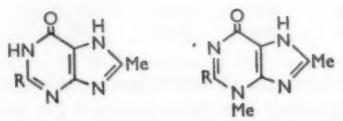
An even more surprising observation is that in an attempted synthesis of 1,2-dihydro-3,8-dimethyl-2-oxopurine the desired intermediate (III) proved unstable. The compound (III) could not be prepared either by condensing 4,5-diamino-3-methyl-6-thiouracil (II) with various salts of acetamidine or by selective thiation of 3,8-dimethylxanthine (no. 9 in Table 1) at carbon atom 6. In the latter procedure, the reaction mixture was decomposed with cold dilute ammonia and the filtrate brought to pH 6 by addition of acetic acid. Only the original thiouracil (II) was obtained crystalline even by this cautious method. It is thus evident that the reaction had proceeded as desired, but that the primary product (III) is unstable and decomposes during either the reaction or the attempted isolation. Similar ring opening occurred in attempts to thiate 3-methyl-8-phenylxanthine. The xanthines (nos. 2 and 8) themselves are, however, perfectly stable under conditions which lead to degradation of 2-hydroxypurine.[8]



Physical Properties.—The 8-methyl group exerts a small bathochromic effect on the absorption maximum. Such slight shifts are well known for methyl substitution in aromatic rings. Apparently the purine skeleton behaves like an aromatic system in transmitting inductive effects, although *N*-methylation may produce either batho- or hypso-chromic changes of $\lambda_{max.}$.[9]

It is noteworthy that 3-methylpurines, in which alkylation has caused fixation of a double bond in position 1,2, exhibit a large bathochromic shift (14—15 mμ) owing to transition from the *ortho*-quinonoid system of hypoxanthine to a *para*-quinonoid structure.[12] This shift is not influenced by a univalent substituent in position 2 (cf. IV—V, where $\lambda_{max.}$ at pH 8 are indicated).

		$\lambda_{max.}$
(IV)	a: R = H	252
	b: R = SMe	265



		$\lambda_{max.}$
(V)	a: R = H	266
	b: R = SMe	280

Table 1 (nos. 2—5) illustrates how in some solvents replacement of a hydroxyl by a mercapto-group decreases and in others increases the R_F value. Comparison of R_F values is possible only if corresponding molecular structures are being considered. *E.g.*, 8-methylxanthine (no. 2) has p*K* 7·5. In solvent C, it is certainly present as monoanion, while in A it forms neutral molecules. On the other hand, 8-methyl-6-thioxanthine (no. 3), with

[12] Bergmann, Levin, Kalmus, and Kwietny-Govrin, *J. Org. Chem.*, 1961, **26**, 1504.

pK ~12·5, exists mainly as neutral molecules even in solvent C. The 2-thio-analogue has pK ~11·5 and the corresponding 2,6-dithio-derivative pK 10·7. A reversal in the order of R_F values within this group of 8-methylpurines, when passing from acid to basic solvents, may therefore be attributed to the different distribution of ionised forms.

Experimental

Ultraviolet spectra were measured in 0·1M-phosphate buffer of pH 8·0, on a Beckman DU spectrophotometer. Paper chromatograms were developed by the descending method, with the solvents specified in Table 1. Spots were located by their fluorescence under a Mineralight ultraviolet lamp (λ ~255 mμ). pK Values were determined by the spectrophotometric method, as modified by Bergmann and Dikstein.[9]

General Condensation Procedure.—A mixture of a 4,5-diaminopyrimidine and 2 equivalents of acetamidine hydrochloride was heated to 180—190°. At this temperature, a homogeneous melt was usually formed and evolution of ammonia started. After reaction had ceased, the dark cake was dissolved in N-sodium hydroxide, the solution decolorised with charcoal, and the product precipitated by acetic acid (to pH ~6). All purines synthesised in the present investigation decomposed above 310°, unless stated otherwise.

The yields of 8-methyl- (no. 1) and 8-phenyl-hypoxanthine (no. 3) and of 2,6-dithio-8-methylxanthine (no. 5) were considerably improved by addition of 2 equivalents of anhydrous sodium acetate to the reaction mixture (see Table 1).

2-Hydroxy-8-methylpurine (cf. I).—(*a*) 4,5-Diamino-2-hydroxypyrimidine[13] (1 g.), acetamidine hydrochloride (1 g.), and anhydrous sodium acetate (0·8 g.) were heated at 140—145° for 20 min. Thereafter the mass solidified. The cake was dissolved in 10% aqueous ammonia and boiled with charcoal. The filtrate was acidified with acetic acid and left in the cold room for 24 hr., whereupon 0·65 g. of crystals was deposited, exhibiting $\lambda_{max.}$ 307 mμ at pH 8·0. Chromatography in solvent A gave 2 spots: (1) R_F 0·32: an extract of this spot had $\lambda_{max.}$ 286—287 mμ (pH 8·0), characteristic of the starting material. (2) R_F 0·43: this material had $\lambda_{max.}$ 313 mμ, corresponding to compound (I). The components were not separated by crystallisation.

(*b*) A suspension of 8-methyl-6-thioxanthine (5 g.) and Raney nickel (1·5 g.; wet weight) in 5% aqueous ammonia (25 ml.) was refluxed for 80 min. The catalyst was filtered off and the solution brought to pH 2 by addition of nitric acid. After 2 months at room temperature, large prisms with a brown tint had crystallised. The substance was identified unequivocally by its absorption spectrum, which is very similar to that of 2-hydroxypurine, and by its conversion into 8-methylxanthine under the influence of mammalian xanthine oxidase.[14] If the solution was acidified with sulphuric acid, the product decomposed quantitatively to the starting material. The result was the same when an ammoniacal solution of compound (I) was evaporated to dryness, the residue extracted with absolute alcohol, and the mixture acidified with 1% of sulphuric acid in absolute alcohol.

8-Methyladenine.[3]—2-Mercapto-8-methyladenine (no. 6) (580 mg.) and Raney nickel (1·5 g.; wet weight) in 5% aqueous ammonia (100 ml.) were refluxed for 2 hr. The solution was filtered while hot. On cooling, prisms (300 mg., 62%) were deposited. The physical properties were identical with those reported by Koppel and Robins.[3] The substance had R_F 0·57, 0·67, and 0·64 in solvents A, B, and C, respectively.

6-Mercapto-8-methylpurine.—8-Methylhypoxanthine (1·3 g.), phosphorus pentasulphide (5 g.), and dry pyridine (50 ml.) were refluxed for 4 hr. The solvent was removed *in vacuo* and the residue extracted with N-sodium hydroxide. After filtration, the solution was brought to pH 6 by glacial acetic acid, boiled with charcoal, again filtered, concentrated *in vacuo*, and left at 0° overnight. The precipitate (1·1 g., 76%) was removed and recrystallised from water as needles, decomp. >310°. This product has been obtained previously by Koppel and Robins[3] by a more devious route; it had $\lambda_{max.}$ (pH 8·0) 232, and 316 mμ and R_F 0·64 in solvent A and 0·71 in solvent C (reddish fluorescence).

3,8-Dimethyl-2-methylmercaptohypoxanthine.—3,8-Dimethyl-2-thioxanthine (1 g.) and methyl iodide (0·7 ml.) were stirred in 0·5N-sodium hydroxide (10 ml.) at room temperature for 30 min., precipitation beginning in 10 min. The *compound* crystallised from water in yellowish lancets,

[13] Kalmus and Bergmann, *J.*, 1961, 760.
[14] Unpublished results.

decomp. 312—315° (0·95 g., 88%), R_F 0·73 in solvent B (Found: C, 45·7; H, 4·6; N, 27·1. $C_8H_{10}N_4OS$ requires C, 45·7; H, 4·8; N, 26·7%).

3,8-*Dimethylhypoxanthine*.—3,8-Dimethyl-2-thioxanthine (2 g.) and Raney nickel (6 g.; wet weight) in 5% ammonia (50 ml.) were refluxed for 2 hr. The filtrate was left at 0° overnight without depositing crystals. After concentration *in vacuo*, the *hypoxanthine* (1·4 g., 83%) was obtained; it crystallised from ethanol as prisms, decomp. ~300°, R_F 0·6 in solvent B (Found: C, 51·1; H, 5·2; N, 33·8. $C_7H_8N_4O$ requires C, 51·2; H, 4·9; N, 34·1%).

Attempted Synthesis of 3,8-*Dimethyl-6-thioxanthine*.—(a) 4,5-Diamino-3-methyl-6-thiouracil (II) and acetamidine hydrochloride or acetate at temperatures between 150° and 200° yielded only starting material and tars. (b) Reaction of 3,8-dimethylxanthine with phosphorus pentasulphide in pyridine, removal of the solvent *in vacuo*, decomposition with cold aqueous ammonia, and adjustment of the pH to 6 produced only the diamine (II). The latter was identified with authentic material by its spectrum ($\lambda_{max.}$ at pH 8·0, 249 and 344 mμ) and its R_F value (0·33 in solvent A).

Conversion of 8-*Methyl*-2,6-*dithioxanthine into* 8-*Methylpurine*.—8-Methyl-2,6-dithioxanthine (1 g.) and Raney nickel (2·5 g.) in 5% aqueous ammonia (50 ml.) were refluxed for 70 min. The catalyst was removed and the filtrate concentrated *in vacuo*. On being left overnight, the solution deposited needles (150 mg., 22%). 8-Methylpurine has $\lambda_{max.}$ at pH 8·0, 266 mμ, R_F 0·75 in solvent A (violet fluorescence). The yield by this method is only about half that reported by Albert and Brown,[8] but the product is at once in pure form.

This study was supported by a grant from the United States National Institutes of Health.

Department of Pharmacology,
The Hebrew University—Hadassah Medical School,
Jerusalem, Israel. [*Received, April 20th*, 1961.]

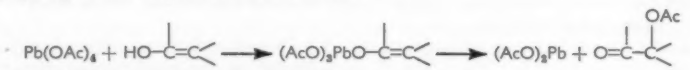
---

881. *Reactions of Ketones with Oxidising Agents. Part I. Catalysis of the Ketone–Lead Tetra-acetate Reaction with Boron Trifluoride.*

By H. B. Henbest, D. N. Jones, and G. P. Slater.

Ketones are acetoxylated by lead tetra-acetate at room temperatures when boron trifluoride is present as catalyst, cholestan-2- and -3-one giving the 3α-acetoxy- (VII) and 2α-acetoxy-ketone (II), respectively. 2α-Acetoxycholestan-3-one isomerises on alumina to 3β-acetoxycholestan-2-one (III); and the fourth ketol acetate of this group, 2β-acetoxycholestan-3-one (IX), has been prepared by oxidation of 2β-acetoxycholestan-3α-ol. The ultraviolet absorption of 2β-acetoxycholestan-3-one is unusual, the axial acetoxy-group giving a small hypsochromic shift. The rotatory dispersions of the four acetoxy-ketones are briefly discussed, the most striking feature being the reduced amplitude caused by introduction of an axial acetate group.

One of the reactions of lead tetra-acetate with organic compounds is to introduce an acetoxy-group into a position adjacent to a carbonyl group.[1] Kinetic [2] and other evidence suggests that enolisation of the carbonyl compound can be the first, and largely rate-determining, step of the reaction. In view of the evidence that alcohols react with lead tetra-acetate to give alkoxylead triacetates,[3,4] the enolic form of the carbonyl compound probably gives an ester that decomposes to lead diacetate with intramolecular donation of an acetoxy-group to the adjacent carbon atom:



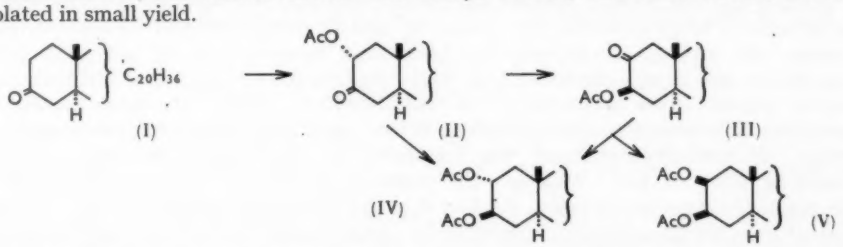
[1] Dimroth and Schweizer, *Ber.*, 1923, **56**, 1375.
[2] Ichikana and Yamakuchi, *J. Chem. Soc. Japan*, 1952, **73**, 415; *Chem. Abs.*, 1953, **47**, 10,474.
[3] Cordner and Pausacker, *J.*, 1953, 102.
[4] Henbest, *Ann. Reports*, 1956, **53**, 146.

XUM

If the carbonyl compound is appreciably enolised (*e.g.*, for β-diketones), reaction with lead tetra-acetate often occurs readily at 10—40°,[1,5,6] although by-products arising from dehydrogenative coupling of the carbonyl compound and indicative, therefore, of a competing radical reaction are sometimes obtained.[5,7] Phenols, like enols, react readily with lead tetra-acetate and *o*- and *p*-acetoxy-compounds are formed;[8] the mechanism is probably similar to that of the enol reaction although the route by which the acetate group reaches the *para*-position requires clarification. The easily enolised βγ-unsaturated ketone, cholest-5-en-3-one, reacts with lead tetra-acetate at 15—20°, giving the 4α-acetoxy-compound.[9] Higher temperatures (70—100°) are required for acetoxylation of 3-oxo-Δ^4-steroids and most saturated ketones at convenient rates.[10,11] As radical and other species are formed when lead tetra-acetate is heated to 70° and above,[12] use of the normal reaction conditions for acetoxylating saturated ketones could result in side reactions, especially if other functional groups, reactive towards radicals, are present. Lower temperatures could probably be used if enolisation could be accelerated, and this led to our trying boron trifluoride as catalyst. This reagent is effective for the acylation of ketones by acid anhydrides,[13] reactions that presumably also involve initial enolisation of the carbonyl compound. Use of many of the usual acidic and basic catalysts is ruled out by their reactions with the quadrivalent lead salt.

Reaction between cholestan-3-one (I) and lead tetra-acetate (1·1 mol.) occurred at 25° if boron trifluoride was added (its ether complex was used). Rates of reaction were similar in ether and acetic acid but greater in benzene. Addition of isopropyl alcohol to the benzene solution slowed the reaction. Oxygen-containing solvents no doubt compete with cholestanone for the boron trifluoride (cf. a similar difference between ether and benzene in the boron trifluoride-catalysed isomerisation of a 9α,11α-epoxy-Δ^7-steroid [14]). In contrast, acetoxylation of cyclohexanone at 80° in the absence of a catalyst is faster in acetic acid than in benzene,[5] the former solvent assisting enolisation.

Chromatography of the product from cholestanone on deactivated alumina (see below) gave the new 2α-acetoxycholestanone (II) as the only isolable acetoxy-ketone; the best yields (50%) were obtained by using benzene or benzene–isopropyl alcohol as reaction solvent. Reactions in ether or acetic acid gave the same acetoxy-ketone, but in the latter solvent some αβ-unsaturated ketone was always formed, and cholest-1-en-3-one was isolated in small yield.

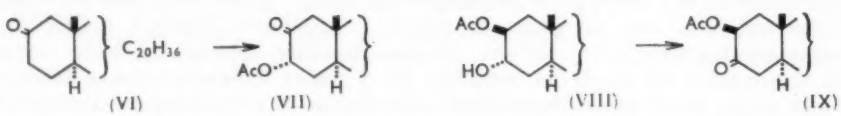


The structure (II) for the acetoxylation product was established by reduction with lithium aluminium hydride: cholestane-2α,3β-diol [15] was the main product [isolated as the

[5] Cavill and Solomon, *J.*, 1955, 4426.
[6] Fuson, Maynert, Tan, Trumbull, and Wassmundt, *J. Amer. Chem. Soc.*, 1957, **79**, 1938.
[7] Cocker and Schwarz, *Chem. and Ind.*, 1951, 390.
[8] Wesseley, Kotlan, and Metlesics, *Monatsh.*, 1954, **85**, 69; Hecker, *Chem. Ber.*, 1959, **92**, 1386; Gold and Schwenk, *J. Amer. Chem. Soc.*, 1958, **80**, 5683.
[9] Fieser and Stevenson, *J. Amer. Chem. Soc.*, 1954, **76**, 1728.
[10] Seebeck and Reichstein, *Helv. Chim. Acta*, 1944, **27**, 948.
[11] Fieser and Romero, *J. Amer. Chem. Soc.*, 1953, **75**, 4716.
[12] Benson, Sutcliffe, and Walkley, *J. Amer. Chem. Soc.*, 1959, **81**, 4488.
[13] Meerwein, *Ber.*, 1933, **66**, 411; Meerwein and Vossen, *J. prakt. Chem.*, 1934, **141**, 149.
[14] Bladon, Henbest, Jones, Lovell, Wood, Woods, Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921.
[15] Henbest and Smith, *J.*, 1957, 926; Shoppee, Jones, and Summers, *J.*, 1957, 3100.

diacetate (IV)] and cholestane-2α,3α-diol was also formed. Adsorption on active alumina converted the acetoxy-ketone (II) into the isomer (III); the isomerisation proceeds by enolisation and acyl group migration *via* a cyclic intermediate (cf. the isomerisation of 4α-acetoxycholest-5-en-3-one on alumina [9]). Reduction of compound (III) with lithium aluminium hydride gave cholestane-2α,3β- and -2β,3β-diol, isolated as diacetates (IV) and (V). 3β-Acetoxycholestan-2-one has been obtained before,[16] by acyloin condensation of a 2,3-seco-diester and acetylation of the resultant ketol mixture. Identity of physical properties and a mixed m. p. determination with a sample provided by Professor J. C. Sheehan confirmed that the products from the two routes were identical. 2α-Acetoxycholestan-3-one has not been described before, the product formed in the reaction of 2α-bromocholestan-3-one with sodium acetate [17] having been shown by indirect evidence [11] to be an inseparable mixture of 2α- and 4α-acetoxycholestanone; a minor product from the acyloin reaction, tentatively regarded [16] as 2α-acetoxycholestanone, was clearly different from the pure compound derived from the acetoxylation reaction.

Our structural assignments were further confirmed by the preparation and properties of the two remaining isomers containing acetate and carbonyl groups at positions 2 and 3. The boron trifluoride-catalysed reaction of cholestan-2-one (VI) with lead tetra-acetate in acetic acid gave an acetoxy-ketone, different from compound (III), and therefore considered to be 3α-acetoxycholestan-2-one (VII) (enolisation towards $C_{(3)}$, not $C_{(1)}$, is preferred for



(VI) (VII) (VIII) (IX)

energy reasons [18,19]). In agreement with structure (VII), a bathochromic shift [140 Å relative to the value for (VI)] was observed in the ultraviolet absorption peak. The remaining isomer, 2β-acetoxycholestan-3-one (IX), was obtained by oxidation of the acetoxy-alcohol (VIII) obtained [20] by acetolysis of 2α,3α-epoxycholestane. It was rapidly isomerised, even on deactivated alumina, to the 2α-acetoxy-compound (II) in which the substituent is equatorial (cf. the similar isomerisation of 2β- to 2α-bromocholestanone [21]).

Each of the four acetoxy-ketones was treated with lead tetra-acetate in acetic acid in the presence of boron trifluoride, the conditions used for acetoxylation of the unsubstituted ketones. 3α- and 3β-Acetoxycholestan-2-one were recovered in 70 and 90% yield, respectively, and there is therefore little doubt that the former compound is the primary reaction product from acetoxylation of cholestan-2-one. Under the same conditions, 2α-acetoxycholestanone was partly recovered (45%) and partly converted into unsaturated ketone. 2β-Acetoxycholestanone was converted in considerable part into material containing more oxygen. Although the presence of some 2α-acetoxycholestanone in this material cannot be excluded, the fact that the 2α-acetoxy-compound is not a major product from the 2β-acetoxy-compound under acetoxylation conditions strongly indicates that the latter compound is not an intermediate in the formation of the 2α-acetoxy-compound from the 3-ketone. The experiments, as a whole, suggest that acetoxylation parallels the bromination of the 2- [19] and 3-ketones, α-attack predominating for steric reasons.

The acetoxylation of cholestan-3-one is also promoted by perchloric acid, the reaction in acetic acid at 25° giving 2α-acetoxycholestanone (14% on non-recovered cholestanone) and unchanged ketone (22%); this method is therefore inferior from the preparative

[16] Sheehan and Erman, *J. Amer. Chem. Soc.*, 1957, **79**, 6050.
[17] Ruzicka, Plattner, and Aeschbacher, *Helv. Chim. Acta*, 1938, **21**, 866.
[18] Henbest, Meakins, and Wood, *J.*, 1954, 800.
[19] Djerassi and Nakano, *Chem. and Ind.*, 1960, 1385.
[20] Fürst and Plattner, *Helv. Chim. Acta*, 1949, **32**, 275.
[21] Alt and Barton, *J.*, 1954, 4284.

point of view. Hydrogen fluoride, which might be formed in traces in the reactions in which boron trifluoride was used as catalyst, was less effective, only a trace of acetoxy-ketone being formed; this is probably due to the conversion of the lead tetra-acetate into lead tetrafluoride.

Rotatory Dispersion and Ultraviolet Absorption of Acetoxy-ketones.—The 3α- and 3β-acetate groups in compounds (VII) and (III) are relatively unhindered and should be particularly suitable for the determination of the effects of axial and equatorial acetoxy-groups on the rotatory dispersion and ultraviolet absorption properties of the 3-ketone group. The 2α-equatorial acetate in compound (II) is also unhindered, but steric overlap of the axial 2β- and 10β-substituents in the acetoxy-ketone (IX) may cause it to show abnormal absorption and rotation properties. Previous work on steroid acetoxy-ketones has been carried out with compounds substituted in ring B, C, or D, where special steric or conformational factors could affect the situation.

Equatorial acetates. Small hypsochromic shifts in the ultraviolet spectrum have been recorded before [22] for steroid ketones with equatorial acetoxy-substituents. The acetate groups in compounds (III) and (II) gave small bathochromic and hypsochromic effects, respectively. They also only caused small changes in the Cotton curves of the ketones.

Axial acetates. In the ultraviolet spectrum, the 3α-acetate group (in VII) gave a bathochromic shift of 14 mμ, compared with shifts of 25 and 32 mμ given, respectively, by chlorine and bromine.[22] The absorption of the other axial acetoxy-ketone (IX) was unusual in giving a small hypsochromic effect, although it may be noted that an axial chlorine in this position shows [22] a smaller bathochromic shift (14 mμ) than usual. Both results suggest that the ring is forced out of the normal chair conformation by overlapping of the 2β- and 10β-axial substituents.

Axial halogen substituents cause the first peak of the rotatory dispersion spectrum to shift by 20—25 mμ to longer wavelengths.[23] Corresponding shifts given by the acetate groups in compounds (VII) and (IX) were 8 mμ and 1 mμ, the latter compound again showing atypical properties. Substitution of (axial) 3α- and 2β-bromine into 2- and 3-ketones, respectively, strongly enhances the positive Cotton curves of the parent ketones, whereas the corresponding acetates (VII) and (IX) gave curves with considerably reduced amplitudes.[24]

Boron trifluoride-catalysed acetoxylations of other oxo-steroids will be reported later.

Experimental

M. p.s were determined on a Kofler block. Rotations were determined for chloroform solutions. Light petroleum refers to the fraction of b. p. 30—40°. Alumina refers to Spence (type H); when necessary, it was deactivated with 5% of 10% acetic acid. Solvents used for reactions were purified by standard methods.

Acetoxylation of Cholestan-3-one (I).—A solution of the ketone (5 g., 1 mol.) and lead tetra-acetate (6·34 g., 1·1 mol.) in acetic acid (222 ml., 300 mol.) containing boron trifluoride–ether complex (9·6 ml., 5·85 mol.) was stirred at 25° under nitrogen. After 145 min. the starch–iodide test for lead tetra-acetate was negative. Isolation with ether gave a yellow oil (5·62 g.) that became semi-solid; its infrared spectrum indicated the presence of acetate and unsaturated ketone groups. It was dissolved in pentane and adsorbed on to Florisil (170 g.). Elution with pentane gave cholestanone, followed by mixtures of this compound with unsaturated ketone (see below). Elution with pentane–benzene (9 : 1) gave *2α-acetoxycholestan-3-one* (II) (2·95 g., 51% based on initial cholestanone), m. p. 123—125° (from acetone–ethanol), $[\alpha]_D$ +57° (Found: C, 78·45; H, 10·75. $C_{29}H_{48}O_3$ requires C, 78·3; H, 10·9%). The fractions containing unsaturated ketone were combined (0·75 g.) and adsorbed on to alumina (75 g.). Elution with pentane–benzene (3 : 1) gave cholestanone (total recovery, 190 mg.). Elution

[22] Cookson, *J.*, 1954, 282; Cookson and Dandegaonker, *J.*, 1955, 352.
[23] Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York, 1960, pp. 118—121.
[24] Amplitude defined by Djerassi and Klyne, *Proc. Chem. Soc.*, 1957, 55.

with pentane–benzene (2 : 1) gave material (402 mg.) ($\lambda_{max.}$ 2350 Å in EtOH) from which cholest-1-en-3-one (100 mg.), m. p. and mixed m. p. 96—98°, was obtained by crystallisation from acetone–ethanol.

αβ-Unsaturated ketone was formed in appreciable amounts only in the reactions in acetic acid. The normal reaction time (to give a negative starch–iodide test) in acetic acid (140—150 min.) was increased to 260 and 400 min. by the presence of 0·33 mol. % of isopropyl alcohol and water, respectively; *ca.* 9% of unsaturated ketone was formed in both of these reactions (*ca.* 10% formed in pure acetic acid). These percentages are calculated by using the molecular extinction (ε 10,700) of cholest-1-en-3-one; the absorption peak (near 2350 Å) of the total unsaturated ketonic product suggests that another compound, possibly cholest-4-en-3-one, is present.

Not all of the lead tetra-acetate dissolved when it was added to the ketone in acetic acid, but the addition of catalyst gave a clear solution.

A mixed m. p. of 2α-acetoxycholestan-3-one with a compound (m. p. 147—149°) tentatively regarded [16] as having this structure gave a value of 121—126°, 137—145° (double m. p.). There was no doubt that the compounds were different.

The reaction between cholestanone (500 mg.) and lead tetra-acetate (1·1 mol) was carried out at 25° in various solvents containing boron trifluoride–ether complex (5·85 mol.). The annexed Table gives the times for complete reaction of the tetra-acetate and the yields of cholestanone and 2α-acetoxycholestanone, determined by chromatographic separation on deactivated alumina, the compounds being eluted respectively with light petroleum and light petroleum–benzene (4 : 1). Use of more active alumina caused the formation of some 3β-acetoxycholestan-2-one (see below).

Solvent (mol.)	Reaction time (min.)	Cholestanone recovered (%)	2α-Acetoxy-cholestanone (%) *
Ether (300)	155	20	36
Benzene (300) + isopropyl alcohol (10) ...	230	14	51
Benzene (300)	47	6	51

* These yields are based on the cholestanone not recovered from the reaction.

Addition of the tetra-acetate to the ketone in dry benzene gave a brown suspension which became a clear solution when the boron trifluoride–ether complex was added.

When 1·5 mol. of lead tetra-acetate was used for the reaction in benzene, the reaction time was 330 min. and 2α-acetoxycholestanone (51%) but no cholestanone was obtained.

The experiment using lead tetra-acetate (1·1 mol.) and benzene as solvent was repeated without the addition of boron trifluoride. After 47 min. the mixture was processed, to give cholestanone (92% recovery). The infrared spectrum of the total crude product gave no indication of the presence of acetoxy-ketone or unsaturated ketone.

Experiments with other catalysts. (*a*) Perchloric acid * (5 mol.) was added to a solution of cholestanone (500 mg., 1 mol.) and lead tetra-acetate (1·1 mol.) in acetic acid (300 mol.) at 25°. The tetra-acetate had reacted after 10 min. Chromatography of the neutral product (538 mg.) gave cholestanone (112 mg., 22%) and 2α-acetoxycholestanone (60 mg., 14% based on unrecovered cholestanone). The alkaline washings from the isolation procedure were acidified and extracted with ether, to give a brown solid (30 mg.). Crystallisation from acetone and from ethyl acetate gave 2,3-seco-5α-cholestane-2,3-dioic acid, m. p. and mixed m. p. 195—196°.

The infrared and ultraviolet absorption of the crude neutral product showed that αβ-unsaturated ketone was absent. Using the longer reaction time of 55 min. led to *ca.* 12% of unsaturated ketone.

(*b*) Cholestanone (500 mg., 1 mol.) and lead tetra-acetate (1·1 mol.) in acetic acid (300 mol.) containing hydrogen fluoride (11 mol.) were stirred at 25° in a Polythene container. After 6·5 hr. the tetra-acetate had not completely dissolved and more acetic acid (256 mol.) and hydrogen fluoride (11 mol.) were added. After 26·5 hr. the test for lead tetra-acetate was still positive, and the product (533 mg.) was isolated as usual. The infrared spectrum showed that a small amount of acetoxy-ketone was present, but chromatography on deactivated alumina (16 g.) gave cholestanone (170 mg.) as the only solid product.

Acetoxylation of Cholestan-2-one (VI).—Boron trifluoride–ether complex (0·66 ml., 5 mol.)

* Perchloric acid (67% in water) was used; it was dehydrated with the calculated amount of acetic anhydride and the acetic acid formed constituted part of the final 300 mol.

was added to cholestan-2-one (400 mg., 1 mol.) in acetic acid (17·78 ml., 300 mol.) at 25°. After 6 hr. more catalyst (0·88 ml., 6·7 mol.) was added; the test for tetra-acetate then became negative after a further hour. Isolation with ether gave a yellow oil (460 mg.) that was dissolved in light petroleum (b. p. 40—60°) (20 ml.). 3α-*Acetoxycholestan-2-one* (VII) (107 mg.), m. p. 145—148°, separated when the solution was kept. The pure acetoxy-ketone had m. p. 148—149° (from acetone–ethanol), $[\alpha]_D$ +57° (Found: C, 78·5; H, 10·7%). Chromatography of the remainder of the product on deactivated alumina (22·5 g.) gave oils (elution with light petroleum) and more 3α-acetoxycholestan-2-one (80 mg.; total yield 40%), m. p. 146—148°.

2β-*Acetoxycholestan-3-one* (IX).—Oxidation of 2β-acetoxycholestan-3α-ol (VIII) (400 mg.; m. p. 115—117°; lit.,[20] m. p. 113°) by the chromic acid in acetone method [25] gave 2β-*acetoxycholestan-3-one* (288 mg., 73%), m. p. 144—146° (from acetone–methanol), $[\alpha]_D$ +94° (Found: C, 78·15; H, 11·05%). The m. p. was depressed to *ca.* 120° on admixture with either 3α- or 3β-acetoxycholestan-2-one.

Acetylation of 2β-acetoxycholestan-3α-ol with pyridine–acetic anhydride gave 2β,3α-diacetoxycholestane, m. p. 141—142° (from acetone–methanol), $[\alpha]_D$ +60° (Found: C, 76·25; H, 10·5. Calc. for $C_{31}H_{52}O_4$: C, 76·2; H, 10·7%). The mixed m. p. with an authentic sample (m. p. 137—138°) was 138—140°.

Light absorption and rotatory dispersion of the acetoxy-ketones.

Acetoxy-ketone	Infrared C=O absorption (cm.$^{-1}$)	Ultraviolet absorption $\lambda_{max.}$ (Å) (log ε)	Rotatory dispersion [φ] peak (Å), [φ] trough (Å)	amplitude ($10^{-2}a$)
(II)	1759, 1740	2800 (1·56)	+3060 (3100) −3560 (2700)	+66
(IX)	1758, 1743	2820 (1·39)	+4370 (3080) −148 (2630)	+45
(III)	1756, 1735	2850 (1·53)	+7300 (3080) −4300 (2680)	+116
(VII)	1756, 1730	2940 (1·62)	+3400 (3180) −1740 (2780)	+52

Infrared spectra were determined for carbon tetrachloride, ultraviolet spectra for ethanol, and rotatory dispersions for methanol solutions.

The Action of Lead Tetra-acetate on the Acetoxy-ketones.—2α-*Acetoxycholestan-3-one.* The acetoxy-ketone (100 mg.) and lead tetra-acetate (127 mg., 1·3 mol.) in acetic acid (4·45 ml., 350 mol.) containing boron trifluoride–ether complex (0·19 ml., 6·8 mol.) were stirred under nitrogen at 25° for 1 hr., the test for lead tetra-acetate remaining strongly positive. Isolation gave a brown oil (94 mg.), containing an αβ-unsaturated ketone (infrared evidence). Crystallisation from acetone gave 2α-acetoxycholestan-3-one, m. p. 121—123° (45 mg., 45% recovery). The ultraviolet spectrum of the mother liquor indicated that cholest-1-en-3-one (8%) had been formed.

3α- and 3β-Acetoxycholestan-2-one were recovered in 89% and 70% yield, respectively, after similar treatment for 1·5 and 2 hr., respectively.

2β-*Acetoxycholestan-3-one.* This was similarly treated with lead tetra-acetate whereupon a compound, m. p. 154—156°, was formed. The constitution of this compound will be discussed in a later paper.

Reactions on Alumina.—2β-*Acetoxycholestan-3-one.* The acetoxy-ketone (210 mg.), dissolved in pentane–benzene (9 : 1), was adsorbed on deactivated alumina (6·4 g.) for 1 hr. Elution with pentane–benzene (9 : 1) gave 2α-acetoxycholestan-3-one (148 mg., 71%), m. p. and mixed m. p. 123—124°.

2β-Acetoxycholestan-3-one (250 mg.) in pentane–benzene (9 : 1) was placed on a column of active alumina (7·5 g.) and similar elution was commenced immediately: 2α-acetoxycholestan-3-one (163 mg., 65%), m. p. and mixed m. p. 123—125°, but no 3β-acetoxycholestan-2-one, was obtained.

2α-*Acetoxycholestan-3-one.* The acetoxy-ketone (150 mg.) in benzene was adsorbed on active alumina (10 g.) for 16 hr. Elution with benzene gave 3β-acetoxycholestan-2-one, m. p. 146—147° (30 mg., 20%), $[\alpha]_D$ +76° (Found: C, 78·8; H, 10·9%), followed by starting material,

[25] Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39.

m. p. 122—129° (67 mg., 45% recovery). A sample (m. p. 138—141°) of 3β-acetoxycholestan-2-one supplied by Professor J. C. Sheehan gave, on admixture with our sample, a m. p. of 141—145°. The mixed m. p. with our sample of 3α-acetoxycholestan-2-one (m. p. 148—149°) gave a depression to 116—130°.

Reduction of 3β-Acetoxycholestan-2-one (III).—The acetoxy-ketone (250 mg.) was reduced with lithium aluminium hydride (100 mg.) in boiling ether (25 ml.) for 20 min. The product was treated with acetic anhydride and pyridine at 20° overnight, and the acetate was chromatographed on deactivated alumina (22 g.). Elution with light petroleum gave 2α,3β-diacetoxycholestane (IV) (30 mg.), m. p. and mixed m. p. 112—113° (from methanol), whilst elution with light petroleum–benzene (19 : 1) gave 2β,3β-diacetoxycholestane (V) (47 mg.), m. p. and mixed m. p. 123—125° (from methanol). These compounds also showed infrared spectra identical with those of authentic samples. Further elution with light petroleum–benzene gave a compound (15 mg.), m. p. 156—158°, which displayed an infrared spectrum consistent with that of an acetoxy-alcohol.

Reduction of 2α-Acetoxycholestan-3-one (II).—This compound (250 mg.) was reduced as in the previous experiment. Acetylation and chromatography on deactivated alumina (14 g.) gave 2α,3β-diacetoxycholestane (IV) [151 mg.; eluted with pentane–benzene (19 : 1)], m. p. and mixed m. p. 112—114°, and 2α,3α-diacetoxycholestane [22 mg.; eluted with pentane–benzene (3 : 1)], m. p. and mixed m. p. 134—136°.

We thank Glaxo Laboratories Ltd. for financial assistance (to G. P. S.), Professor J. C. Sheehan and Dr. G. H. R. Summers for samples, and Professor W. Klyne for rotatory dispersion measurements.

THE QUEEN'S UNIVERSITY OF BELFAST. [*Received, April 20th,* 1961.]

---

882. *Aspects of Stereochemistry. Part XVIII.* Synthesis of the 10-Methyldecalin-2,9-diols.*

By H. B. HENBEST and J. MCENTEE.

The four geometrical isomers of 10-methyldecalin-2,9-diol have been prepared from 10-methyl-$\Delta^{1(9)}$-octalone, the *cis*-diaxial *trans*-fused diol (IX) being required for study of the hydrolysis of its monoesters.

HYDROLYSIS of esters can be assisted by intramolecular participation of a suitably placed nucleophilic or electrophilic substituent. Neighbouring hydroxyl groups are the most important examples of the latter type, and acceleration of hydrolysis has been noted with monoesters of cholestane-*cis*-3,5-diols [1] and with some hydroxy-esters derived from cevine and germine.[2] The hydroxyl group of a neighbouring carboxyl group apparently assists the hydrolysis of the hydrogen succinate of salicylic acid.[3]

The infrared spectra of the monoacetates of the two steroid *cis*-diaxial diols showed [1] hydrogen bonding between the 5-hydroxyl group and the alkyl-oxygen of the 3-acetate, whereas hydroxyl groups normally form bonds with the carbonyl-oxygen of esters when there are no stereochemical restrictions. Intramolecular hydrogen bonding does not occur in the more flexible monoesters of acyclic 1,3-diols. Pronounced hydrogen bonding to the ether-oxygen and acceleration of ester hydrolysis may therefore be confined to compounds in which the two groups are held close together by the molecular structure.

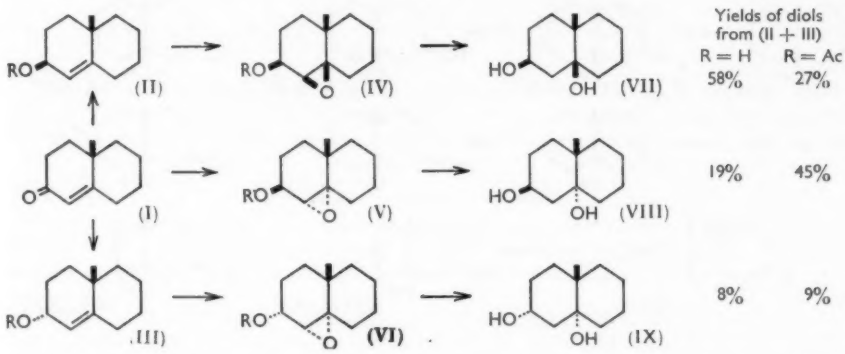
Serine constitutes part of the active site of chymotrypsin and some other hydrolytic enzymes, and the hydroxyl group of this amino-acid may be involved in the reactions

* Part XVII, *J.*, 1960, 3575.

[1] Henbest and Lovell, *Chem. and Ind.*, 1956, 278; *J.*, 1957, 1965.
[2] Kupchan and Johnson, *J. Amer. Chem. Soc.*, 1956, **78**, 3864; Kupchan and Narayanan, *ibid.*, 1959, **81**, 1913.
[3] Morawetz and Oreskes, *J. Amer. Chem. Soc.*, 1958, **80**, 259.

XUM

catalysed by these enzymes.[4] The assistance given to the hydrolysis of steroid axial acetates by neighbouring hydroxyl groups may therefore be a process related to, but simpler than, those occurring in enzyme-catalysed reactions. In order to be able to make physicochemical comparisons, particularly kinetic studies in aqueous media, the synthesis of monoesters of bicyclic diols related to the 3,5-dihydroxy-steroids was undertaken. Esters of the particularly rigid diaxial diol (IX) were especially required.



The bicyclic ketone (I), prepared from 2-methylcyclohexanone, was reduced by lithium aluminium hydride to a mixture of alcohols (II and III). Reduction of relatively unhindered unsaturated ketones often yields the quasiequatorial alcohol as the main product. Application of this rule to the reduction of ketone (I) is made difficult by the fact that both alcohols (II and III; R = H) can assume conformations in which the hydroxyl groups are quasiequatorial. The further reactions of the alcohol mixture showed that the ratio of (II) : (III) was about 9 : 1.

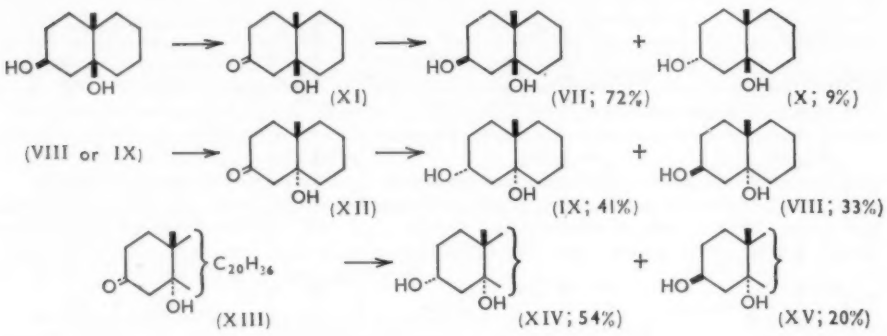
The allylic alcohol mixture (II and III; R = H) was treated with perbenzoic acid, and the epoxide product was reduced with lithium aluminium hydride to a mixture of diols. Chromatography gave three of the four possible diols in crystalline form. The same three diols (two of them in different proportions, see below) were obtained from the mixed acetates (II and III; R = Ac) by successive reactions with peracid and lithium aluminium hydride. The yields of diols are given alongside the structures (VII, VIII, and IX) which are based on the following chemical and spectroscopic evidence.

The steroid (cholestane) analogues of compounds (II; R = H and Ac) give, on epoxidation and reduction, cholestane-3β,5β- and -3β,5α-diol, respectively.[5] The bicyclic alcohol and acetate mixtures did not give the same isomer as major product. The two major products here differ in configuration at $C_{(9)}$ because they gave different ketols on oxidation, but they do not differ in configuration at $C_{(2)}$ (see below), both being derived ultimately from the alcohol (II; R = H). This evidence and the analogy with the steroid series suggest that these two diols have structures (VII) and (VIII). The ketols, obtained by oxidation with chromic acid, must then be formulated as (XI) and (XII), respectively.

The third diol, obtained in similar small yield starting from either the allylic alcohol or the allylic acetate mixture, had the same configuration as diol (VIII) at the angular position $C_{(9)}$ as it was oxidised to the same ketol (XII); structure (IX) is assigned to this diol. The yields of diol (IX) by the alcohol and the acetate route were almost identical, as they depend only on the proportion of the 2α-alcohol (III; R = H) in the original mixture obtained by reduction of ketone (I). The combined yields of the diols (VII and VIII), 77% from the alcohol mixture and 72% from the acetate mixture, represent the proportion of 2β-alcohol (II; R = H) in the original mixture.

[4] Westheimer, *Proc. Nat. Acad. Sci. U.S.A.*, 1957, **43**, 969.
[5] Henbest and Wilson, *J.*, 1957, 1958.

Reduction of ketol (XII) with lithium aluminium hydride gave the diols (VIII) and (IX) in 33 and 41% yield, respectively. Reduction of ketol (XI) gave a high yield of diol (VII) and a small amount of the fourth isomer (X). The compounds with *cis*-hydroxyl groups were the major products from each of these reductions. [The sequence (VIII) ⟶ (XII) ⟶ (IX) gave a method for obtaining more of this required diaxial compound; it



was only obtained in small yield from the epoxy-alcohol mixture (IV, V, VI; R = H).] Similarly, reduction of 5α-hydroxycholestan-3-one (XIII) yielded the *cis*-3α,5α-diol (XIV) as the chief product, although in the absence of the 5α-hydroxyl group, reduction (of cholestanone) gives the 3β-alcohol in 79% yield.[6] The effect of the angular hydroxyl group may be steric, its bulk (possibly as an aluminohydride complex), relative to hydrogen, inhibiting α-approach of reagent. Alternatively, an intramolecular polar effect may be operating of the kind recently discovered in the study of reduction of chloro-ketones by complex hydrides.[7]

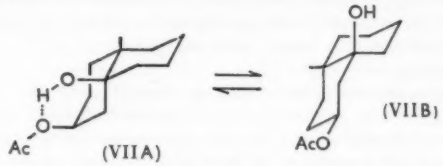
The configurations of the 9-hydroxyl groups in the diols rest largely, as discussed above, on the analogy between the formation of the different main products and the corresponding reactions established in the steroid series. In steroids, the configuration at $C_{(5)}$ of 5-hydroxy-3-ketones may be established by their different rates of dehydration (5β faster) under alkaline conditions, but the method could not be applied to the bicyclic ketols (XI and XII) as they were dehydrated at very similar rates. However, the ease of dehydration of the two ketols (XI) and (XII) provides confirmatory evidence for the assigned structures [containing O=C–CH–C(OH)< groups], and hence for the configuration of the hydroxyl groups at $C_{(2)}$ and $C_{(9)}$ in the original diols. As expected from the given structures, acetylation of each of the four diols under mild conditions gave a (crystalline) monoacetate.

Intramolecular hydrogen bonding in diols should reduce the strength of their adsorption on alumina. Thus, on chromatography, the *cis*-diols, (VII) and (IX), were eluted before the *trans*-compound (VIII). The 2α,9α-diol (IX), containing the strongest hydrogen bond (infrared evidence below), was eluted before the 2β,9β-diol (VII).

We thank Mr. F. Dalton and Dr. G. D. Meakins (Oxford) for determining the infrared spectra of compounds described in this paper. The results, which they will be reporting in detail later, are in accord with the structures assigned above to the diols and ketols. The *trans*-compound (VIII) does not give a peak below 3600 cm.$^{-1}$ but both *cis*-diols (VII and IX) give well-defined peaks (at 3522 and 3532 cm.$^{-1}$, respectively) due to intramolecular hydrogen bonding. The acetates of the *cis*-diols show significant differences: the acetate from (IX) can only exist in one all-chair conformation and gives a single hydroxyl peak (at 3598 cm.$^{-1}$) due to chelation,[1] but the acetate from (VII) gives two

[6] Nace and O'Connor, *J. Amer. Chem. Soc.*, 1951, **73**, 5824.
[7] Combe and Henbest, unpublished work.

hydroxyl peaks, one chelated (at 3599 cm.$^{-1}$) and one unchelated (at 3622 cm.$^{-1}$), corresponding to the two possible conformations, diaxial (VIIA) and diequatorial (VIIB), that this compound can adopt.



(VIIA) (VIIB)

Kinetic studies, being carried out in collaboration with Dr. D. T. Elmore, show that the axial acetate of diol (IX) is hydrolysed more rapidly than the equatorial acetate of diol (VII) under alkaline conditions. Details will be reported later.

Experimental

M. p.s were determined on a Kofler block. Light petroleum refers to the fraction of b. p. 40—60°. Alumina (Spence, type H) was deactivated with dilute acetic acid.[8] The αβ-system of nomenclature [9] is used for denoting geometrical configuration of compounds, all of which are racemic.

Reduction of 10-*Methyl*-$\Delta^{1(9)}$-2-*octalone* (I).—The ketone (10·2 g.) in dry ether (25 ml.) was heated under reflux with stirring for 3 hr. with lithium aluminium hydride (2·4 g.) in dry ether (25 ml.), and then stirred overnight at 20°. Water was slowly added; the ether and the aqueous layer were decanted from the residual slurry which was washed with ether, and the combined ether extracts were dried ($MgSO_4$) and evaporated. Distillation in a short-path still gave the alcohol mixture (II and III; R = H) that was redistilled into fractions (total 9·1 g., 90%), b. p. 73·5—76°/0·2 mm., n_D^{23} 1·5130—1·5140 (Found: C, 79·5; H, 10·6. Calc. for $C_{11}H_{18}O$: C, 79·45; H, 10·9%).

The alcohol (5·75 g.) and acetic anhydride (5 ml.) in dry pyridine (20 ml.) were kept overnight at 20°. Ice-cold 5% sulphuric acid was slowly added until the mixture was acid. The product was isolated with ether and distilled to give the acetate mixture (II and III; R = Ac) (6·65 g., 92%), b. p. 68·5—71°/0·07 mm., n_D^{24} 1·4906—1·4913 (Found: C, 75·15; H, 9·65. Calc. for $C_{13}H_{20}O_2$: C, 74·95; H, 9·7%).

Reaction of the 10-*Methyl*-$\Delta^{1(9)}$-*octalin*-2-*ols* (II *and* III; R = H) *with Perbenzoic Acid*.—The alcohol mixture (3·0 g.) in dry ether (20 ml.) and ethereal 0·48M-perbenzoic acid (45 ml.) were mixed at 0°. After 30 hr. at 0°, reaction was complete. Calcium hydroxide (40 g.) was added, and the mixture was shaken till neutral. The product (2·8 g.) was isolated with ether and distilled in the presence of a trace of calcium hydroxide, to give the mixture of epoxy-alcohols (2·46 g., 74%), b. p. 69—71°/0·04 mm., n_D^{25} 1·4990—1·5000 (Found: C, 72·6; H, 9·9. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·95%).

Reaction of the Acetates (II *and* III; R = Ac) *with Perbenzoic Acid*.—The acetate mixture (6·5 g.) in dry benzene (20 ml.) was mixed at 0° with a 0·46M-solution (80 ml.) of perbenzoic acid in benzene. After 24 hr. at 0°, reaction was complete. The solution was shaken with calcium hydroxide (60 g.) until neutral, and the product was isolated with benzene. Distillation in the presence of a trace of calcium hydroxide gave the epoxy-acetate mixture (6·1 g.), b. p. 83—86°/0·2 mm., n_D^{20} 1·4840—1·4850 (Found: C, 69·8; H, 8·85. Calc. for $C_{13}H_{20}O_3$: C, 69·6; H, 9·0%).

Reduction of the Epoxy-alcohol Mixture.—The mixture (2·25 g.) in dry ether (25 ml.) was heated under reflux with stirring for 3 hr. with lithium aluminium hydride (0·5 g.) in dry ether (25 ml.), and then stirred overnight at 20°. Ethyl acetate (50 ml.) was slowly added, followed by ice-cold 5% sulphuric acid. The aqueous layer was saturated with sodium chloride, and the product was extracted with ethyl acetate. These extracts were washed and dried ($MgSO_4$), to give the diols (2·13 g.). This was dissolved in light petroleum (b. p. 60—80°) (6 ml.) and adsorbed on deactivated alumina (250 g.). Elution with light petroleum–benzene gave a gum (150 mg.). Elution with benzene–ether (9 : 1) gave 10β-*methyldecalin*-2α,9α-*diol* (IX) (168 mg.,

[8] Farrar, Hamlet, Henbest, and Jones, *J.*, 1952, 2657.
[9] Henbest, Smith, and Thomas, *J.*, 1958, 3293.

9%), m. p. 124—128° (m. p. 130—131·5° after crystallisation from isopropyl ether) (Found: C, 71·5; H, 10·85. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·95%) and then the 2β,9β-*diol* (VII) (1·225 g., 68%), m. p. 93—97° (m. p. 98·5—100° after crystallisation from isopropyl ether) (Found: C, 72·0; H, 10·75%). Ether eluted the 2β,9α-*diol* (VIII) (415 mg., 22%), m. p. 154—159° (m. p. 161·5—162·5° after crystallisation from ethyl acetate) (Found: C, 71·7; H, 10·95%). For analyses of these diols and the fourth diol, samples were dried in a high vacuum at 40° immediately before weighing.

Reduction of the Epoxy-acetate Mixture.—The mixture (6 g.) in dry ether (40 ml.) was heated under reflux with stirring for 3 hr. with lithium aluminium hydride (1·0 g.) in dry ether (40 ml.). The diols (4·85 g.) were isolated with ethyl acetate as in the preceding experiment. Part (1·15 g.) was stirred with light petroleum–benzene (1 : 1) (4 ml.) to give the relatively insoluble *trans*-diol (VIII) (421 mg.), m. p. 160—162°. The soluble part was adsorbed on deactivated alumina (100 g.) and separated into *cis*-diol (IX) (107 mg., 11%), *cis*-diol (VII) (313 mg., 33%), and *trans*-diol (VIII) (96 mg.; total yield 517 mg., 56%) as in the previous experiment. The pure diols obtained by crystallisation had the same m. p.s as those previously obtained.

Oxidation of 10β-*Methyldecalin*-2β,9α-*diol* (VIII).—Chromic acid (*ca.* 8N; [10] 0·30 ml.) was added in 2 min., with swirling, to the diol (200 mg.) in " AnalaR " acetone (20 ml.) at 20°. After a minute water was added and the product (180 mg.) was isolated with methylene chloride. Two crystallisations from isopropyl ether gave 9α-*hydroxy*-10β-*methyl*-2-*decalone* (XII) (134 mg., 67%), m. p. 162—163° (mixed m. p. with starting material, 140—147°) (Found: C, 72·5; H, 9·8. $C_{11}H_{18}O_2$ requires C, 72·5; H, 9·95%).

Oxidation of 10β-*Methyldecalin*-2β,9β-*diol* (VII).—The diol (360 mg.) in " AnalaR " acetone (30 ml.) was treated with 8N-chromic acid (0·55 ml.) as in the previous experiment. The product (328 mg.) was isolated as before and crystallised from isopropyl ether, to give 9β-*hydroxy*-10β-*methyl*-2-*decalone* (XI) (202 mg., 56%), m. p. 124—125° (Found: C, 72·6; H, 9·85%).

Dehydration of the Ketols (XI) *and* (XII).—Solutions of the ketols (1 mg.) in pure dioxan (100 ml.) were dehydrated at 20° with 0·1% methanolic potassium hydroxide (100 ml.) to 10-methyl-$\Delta^{1(9)}$-2-octalone, rates being followed by the rise in intensity at 2420 Å. The dehydrations proceeded at similar rates; after 24 hr. the solutions from the ketols (XI and XII) showed ε_{2420} of 10,280 and 10,370 respectively [pure (I) has ε_{2420} 14,900]. Under the same conditions 5α-hydroxycholestan-3-one gave a solution with ε_{2420} 11,400 (pure cholest-4-en-3-one has ε_{2420} 16,000).

Reduction of 9α-*Hydroxy*-10β-*methyl*-2-*decalone* (XII).—The ketol (245 mg.) in dry ether (25 ml.) was heated under reflux for 3 hr. with lithium aluminium hydride (25 mg.). The excess of hydride was decomposed with wet ether, and the product (225 mg.) was isolated with ether. It was warmed with light petroleum–benzene (1 : 1) (2 ml.), leaving the 2β,9α-diol (VIII) (55 mg.), m. p. and mixed m. p. 160—163°. The soluble portion (170 mg.) was chromatographed on deactivated alumina (20 g.); elution with benzene–ether (9 : 1) gave the 2α,9α-diol (IX) (93 mg., 41%), m. p. 127—130°; and elution with ether gave more of the 2β,9α-diol (VIII) (20 mg.; total yield 75 mg., 33%), m. p. 155—159°. Gummy material (50 mg.) was eluted before the diols.

Reduction of 9β-*Hydroxy*-10β-*methyl*-2-*decalone* (XI).—The ketol (140 mg.) in dry ether (25 ml.) was heated under reflux for 3 hr. with lithium aluminium hydride (20 mg.). The product (124 mg.) was isolated with ether as in the preceding experiment and chromatographed on deactivated alumina (15 g.). Elution with benzene–ether (9 : 1) gave the 2β,9β-diol (VII) (73 mg.), m. p. and mixed m. p. 97—99°. Elution with ether gave a mixture (31 mg.), m. p. 96—112°, which, on chromatography on deactivated alumina (3 g.), gave on elution with benzene–ether (9 : 1) the 2β,9β-diol (VII) (15 mg.; total yield 88 mg., 72%), m. p. 95—98°, and with ether the 2α,9β-*diol* (X) (12 mg., 9%), m. p. 141—142° (after sublimation at 100°/0·5 mm.) (Found: C, 71·3; H, 10·55%). Viscous material (19 mg.) was eluted with benzene before the diols appeared.

Reduction of 5α-*Hydroxycholestan*-3-*one* (XIII).—The keto-steroid (250 mg.) in dry ether (25 ml.) was heated under reflux for 3 hr. with lithium aluminium hydride (15 mg.). The excess of hydride was decomposed with wet ether, and the residual slurry was washed with ether. The combined ether extracts were dried ($MgSO_4$), and the resulting product (236 mg., 94%) was chromatographed on deactivated alumina (30 g.). Elution with benzene–ether (9 : 1) gave cholestane-3α,5α-diol (XIV) (135 mg., 54%), m. p. and mixed m. p. 195—198°. Elution

[10] Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39.

with ether gave cholestane-3β,5α-diol (XV) (50 mg., 20%), m. p. and mixed m. p. 223—224° (crystallised from isopropyl ether). Viscous material (43 mg.) was eluted with benzene before the steroid diols.

2α-*Acetoxy*-10β-*methyldecalin*-9α-*ol*.—The diol (IX) (350 mg.) in dry pyridine (7 ml.) with acetic anhydride (2·1 ml.) was kept overnight at 40°. Ice was added and the product was isolated with ether. Sublimation at 60°/0·2 mm. gave the *acetoxy-alcohol* (397 mg., 92%), m. p. 40·5—41·5° (Found: C, 68·65; H, 10·1. $C_{13}H_{22}O_3$ requires C, 69·0; H, 9·8%). Similar acetylation of the diol (X) gave 2α-*acetoxy*-10β-*methyldecalin*-9β-*ol* (65%), m. p. 53° (from isopropyl ether) (Found: C, 69·2; H, 9·65%).

2β-*Acetoxy*-10β-*methyldecalin*-9α-*ol*.—The diol (VIII) (1·0 g.) in dry pyridine (20 ml.) with acetic anhydride (6 ml.) was kept overnight at 20°. The product was isolated with ether and sublimed at *ca.* 100°/0·5 mm., to give the *acetoxy-alcohol* (1·12 g., 92%), m. p. 103·5—104·5° (Found: C, 68·6; H, 9·55%).

Similar acetylation of the diol (VII) (660 mg.) gave 2β-*acetoxy*-10β-*methyldecalin*-9β-*ol* (736 mg., 91%), m. p. 91·5—92·5° (Found: C, 69·0; H, 9·7%). The mixed m. p. with diol (VIII) was 77—88°.

The authors are grateful to Gallahers Ltd., Belfast, for financial assistance (to J. M.).

THE QUEEN'S UNIVERSITY OF BELFAST. [*Received, April 24th,* 1961.]

---

883. *Effect of Pressure on the Transport of Non-electrolytes through Ion-selective Membranes.*

By J. W. JARVIS and F. L. TYE.

The transport number of glycerol in a Permaplex C-10 ion-selective membrane is shown to be markedly reduced by the application of a pressure differential across the membrane. The mechanism of the phenomenon is discussed.

THE removal of electrolytes from non-electrolytes or from substances of zero net charge can be conveniently carried out by electrodialysis through ion-selective membranes. Although the method has been widely practised [1] it has only recently been appreciated that substantial amounts of non-electrolyte may be lost by passage through the membranes.[2] Previous work [2] demonstrated that transport of glycerol and D-glucose through Permaplex C-10 and A-10 membranes (The Permutit Co., Ltd.) occurred largely by electro-osmosis. A simple theoretical treatment showed that the percentage loss of non-electrolyte by electro-osmosis was directly proportional to the reduction in electrolyte concentration. It follows that the percentage loss of electrolyte can be reduced simply by diluting the solution before electrodialysis, as in this way the reduction in electrolyte concentration is made smaller for the same total amount of electrolyte removed. This procedure naturally leads to the non-electrolyte's being obtained as a solution more dilute than the original.

It was noted previously [2] that an osmotic flow of water through the membranes in the reverse direction reduced the transport of non-electrolyte. Hence it seemed possible that reversed water flow caused by a pressure differential across the membrane might also reduce non-electrolyte transport. The purpose of this paper is to report the effect of pressure on the transport number of glycerol in a Permaplex C-10 membrane.

Experimental.—The materials, analysis, and general procedure were as described previously.[2] The cell also was similar except that provision was made for a pressure differential to be applied across the central cation-selective membrane. To prevent bowing, this membrane

[1] *Inter al.*, Lightfoot and Friedman, *Ind. Eng. Chem.*, 1954, **46**, 1599; Wingerd and Block, *J. Dairy Sci.*, 1954, **27**, 932; Burianek and Slechtova, *Listy Cukr.*, 1959, **75**, 62, 82.
[2] Jarvis and Tye, *J.*, 1960, 620.

was supported on the low-pressure side by a sheet of $\frac{1}{8}$″ expanded polyvinyl chloride (Expanded Metal Co., Ltd.) resting against Perspex ribs which traversed the centre compartment.

Runs were carried out at current densities of 4·4 and 22 mA/cm.^{2} and, at each current density, pressure differentials across the cation-selective membrane of 0, 32, and 133 cm. of water head were used. The pressure head was always such that the flow of water through the membrane caused by the head was in a direction opposite to the movement of non-electrolyte. The solution donating the cations and non-electrolyte to the cation-selective membrane was initially 1·09M in glycerol and 2·3M in sodium chloride. The glycerol concentration changed by less than 8% during a run and the concentration of sodium chloride decreased to 2·06 $\pm$ 0·03M and 1·3 $\pm$ 0·15M in the low and high current-density runs, respectively. The average concentrations of the solution receiving the cations and glycerol from the cation-selective membrane were 0·22 $\pm$ 0·02M and 0·51 $\pm$ 0·05M with respect to sodium chloride in the low and high current-density runs and always less than 0·04M in glycerol.

The results are expressed as transport numbers (t) of glycerol, *i.e.*, moles of glycerol passing through the cation-selective membrane per faraday.

Results and Discussion.—The results, given in the Table, show that a pressure differential (Δp) has a very marked effect on the transport of glycerol through the membrane. Quite moderate pressure differentials reduced the glycerol transport more than ten-fold. The effect was due to the small liquid flow, caused by the pressure differential, which passed through the membrane in the direction opposite to that in which the glycerol was being transported. The liquid flow was not actually through the ion-exchange particles of the heterogeneous membrane but rather through paths between the exchange resin and the inert matrix. The glycerol was removed from the exchange resin through which it was being transported by partition with the liquid in the space between the resin particles and the inert matrix. In effect the resin was subjected to a countercurrent washing. The presence of interstices between the ion-exchange resin and the inert matrix has been demonstrated by Hale and McCauley [3] for membranes similar to that used in this study.

Transport numbers (t) for glycerol on electro-osmosis against a pressure differential (Δp; in cm. of H_2O).

Δp	0	32	133
(t at Δp)/(t at $\Delta p = 0$): at 4·4 milliamp./cm.^{2} ...	1·0	0·13	0·02
at 22 milliamp./cm.^{2} ...	1·0	0·42	0·04

Evidence for such a mechanism was obtained from experiments with a Permaplex C-20 membrane (The Permutit Co., Ltd.). This membrane is identical with Permaplex C-10 except that a reinforcing web of inert material is incorporated during manufacture. As a result when the membrane swells in water, the swelling is restricted in the plane normal to membrane thickness, and the development of paths right through the membrane between resin and matrix is considerably reduced. In consequence the water permeability of Permaplex C-20 is a power of ten less than that for Permaplex C-10. Further, the application of a pressure differential of 133 cm. of water head across a Permaplex C-20 membrane had no effect on the transport number of glycerol. This demonstrates that the reduction in transport number of glycerol in the case of the Permaplex C-10 membrane was due to liquid flow between the resin and inert matrix and not to a much smaller flow through the ion-exchange resin itself.

The effect of current density is qualitatively understandable. At the lower current density the rate at which glycerol was being transported was lower, so that a smaller liquid flow and hence a lower pressure differential was necessary to bring about a similar reduction in glycerol transport.

The use of a small flow from the receiving solution to the donating solution to reduce the transport number of glycerol must reduce the effective selectivity of the membrane by transporting salt in the direction opposite to that transported by the electric current. The sodium chloride transferred by liquid flow is VN g.-equiv. sec.$^{-1}$ cm.$^{-2}$ where V is the

[3] Hale and McCauley, *Trans. Faraday Soc.*, 1961, **57**, 135.

flow in l. sec.$^{-1}$ cm.$^{-2}$ and N is the normality of the sodium chloride in the receiving solution. The decrease in transport number of the counter-ion is thus VNF/i, where F is the faraday and i is the current density in amp. cm.$^{-2}$. If the reduction in counter-ion transport number is to be limited to 0·1, then VN/i must be less than $1{\cdot}04 \times 10^{-6}$ g.-equiv. coulomb^{-1}. Separate experiments showed the flow through the Permaplex C-10 membrane to be proportional to the pressure differential and equal to $6{\cdot}7 \times 10^{-11}$ l. sec.$^{-1}$ cm.$^{-2}$ for a differential of 1 cm. of water head. From this it was calculated that the maximum value of VN/i in the present work was $0{\cdot}45 \times 10^{-6}$ g.-equiv. coulomb^{-1}. Therefore changes in the cation membrane selectivity should have been small and the experimental results confirmed that this was so.

The authors thank Dr. T. R. E. Kressman for his interest in the work.

THE PERMUTIT CO., LTD., GUNNERSBURY AVENUE,
LONDON, W.4.

[*Received, April 24th,* 1961.]

---

884. *Radiation Chemistry of Organic Halogen Compounds. Part I. The Action of γ-Radiation on Chlorinated Ethylenes.*

By W. MILLER, (the late) W. H. STAFFORD, W. H. TAYLOR, D. LEAVER, and A. H. MCQUILLAN.

Both stereoisomers of 1,2-dichloroethylene polymerise under the influence of γ-radiation but only the *trans*-isomer gives a solid polymer. Trichloroethylene produces lower yields of oligomers, chloroacetylenes, and a solid decachlorohexane. Tetrachloroethylene gives the lowest yield of oligomer and also hexachloroethane, hexachlorobuta-1,3-diene, and hexachloro-4-dichloromethylenecyclopentene.

NUMEROUS attempts to polymerise 1,2-dichloro- (reviewed by Weale [1]) and trichloroethylenes,[2] by heat, pressure, peroxides, or ultraviolet light, have met with only limited success and, when the present work started, there was little information concerning the action of ionising radiations on these compounds. Futrell and Newton [3] recently reported an intensive study of the action of α-particles, electrons, and γ-rays on *cis*- and *trans*-1,2-dichloroethylene and Newton [4] has studied the α-radiolysis of trichloroethylene. We [5] too have examined the behaviour of these compounds, and of tetrachloroethylene, when exposed to ^{60}Co γ-radiation.

Irradiation of *cis*-1,2-dichloroethylene yielded mainly a mixture of liquid oligomers, separable by fractional distillation, and smaller quantities of involatile waxes. The *trans*-isomer, under similar conditions, gave these products in smaller yield and also a considerable amount of a solid polymer. Hydrogen chloride was produced from both compounds, and isomerisation, in both instances, was negligible.

The physical constants of the dimer were in good agreement with those given by Frank and Blackham [2c] for 1,3,4,4-tetrachlorobut-1-ene obtained by peroxide-initiated polymerisation of 1,2-dichloroethylene. The geometrical isomers of this product were separated by gas–liquid chromatography and the configurations were established by examination of the infrared spectra. The less volatile compound showed a strong absorption at 936 cm.$^{-1}$ which was absent from the spectrum of the other isomer. Haszeldine [6]

[1] Weale, *J.*, 1952, 2223.
[2] (*a*) F.P. 814,423/1937; (*b*) F.P. 841,728/1939; (*c*) Frank and Blackham, *J. Amer. Chem. Soc.*, 1950, **72**, 3283.
[3] Futrell and Newton, *J. Amer. Chem. Soc.*, 1960, **82**, 2676.
[4] Newton, U.S.A.E.A. Report UCRL–3240.
[5] Cooper and Stafford, Proc. Second United Nations Internat. Conf. on Peaceful Uses of Atomic Energy, United Nations, New York, 1959, Vol. XXIX, p. 118.
[6] Haszeldine, *Nature*, 1951, **168**, 1028.

and Kitson [7] have reported, and we confirm, that the characteristic absorption at 960—970 cm.$^{-1}$ (CH out of plane deformation) normally observed for *trans*-olefins is shifted to about 935 cm.$^{-1}$ for *trans*-CH:CHCl and CH:CHBr groups; we therefore assign the *trans*-configuration to the less volatile isomer. The *cis*-isomer had a strong absorption at 1239 cm.$^{-1}$ which was absent or very weak for the *trans*-isomer. A third, very minor component, which was detected and concentrated in less volatile fractions of the dimer, had an infrared absorption at 855 cm.$^{-1}$ (possibly C:CH_2), suggesting that it might be 2,3,4,4-tetrachlorobut-1-ene. Futrell and Newton [3] also found two main components of the tetrachlorobutene fraction and detected three minor ones.

Production of a solid polymer in high yield from 1,2-dichloroethylene has not previously been observed although various authors [1] have obtained small quantities by other methods of polymerisation and have noted that this polymer is produced only, or in greater amount, from the *trans*-isomer. Our preliminary experiments,[5,8] carried out with monomer which had not been rigorously purified and at a comparatively low dose rate (~10^{16} ev ml.$^{-1}$ min.$^{-1}$), indicated that about 75% of the total polymer produced was solid, but in subsequent experiments, under a wide variety of conditions, sometimes approximating to those of the preliminary work, we were unable to achieve such a high yield of the solid. The percentage of solid polymer was normally in the range 9—25% of the total and increased slowly with increasing dose, although the total yield of polymer decreased under the same conditions (see Table). This result suggests that a proportion of the liquid polymers formed initially is incorporated into the solid as polymerisation proceeds.

Yields of hydrogen chloride and polymer produced by γ-irradiation of chlorinated ethylenes.

Dose rate (10^{17} ev ml.$^{-1}$ min.$^{-1}$)	Total dose (10^{20} ev ml.$^{-1}$)	G(HCl) (molecules per 100 ev)	G(total polymer) [d]	Solid in total polymer (%)
		(i) trans-1,2-*Dichloroethylene*		
4·36 [a]	0·95	1·2	239	9·7
,,	1·91	1·0	236	11·2
,,	3·82	1·0	229	21·1
0·78 [b]	2·32	—	225	18·8
,,	3·58	—	221	19·9
,,	6·00	—	210	22·1
,,	8·35	—	207	23·4
,,	11·03	—	204	24·8
		(ii) cis-1,2-*Dichloroethylene* [a]		
4·36	3·25	1·5	134	0
,,	4·87	1·2	142	0
,,	6·50	1·5	138	0
		(iii) *Trichloroethylene* [a]		
4·88	5·48	4·4	31	—
,,	10·96	4·5	34	—
,,	21·92	3·7	34	—
		(iv) *Tetrachloroethylene* [b, c]		
0·9	4800		9	

[a] Irradiated in sealed evacuated ampoules. [b] Irradiated in annular vessels without complete exclusion of air. [c] Approximate values. [d] Estimated as number of monomer molecules removed per 100 ev absorbed.

Futrell and Newton [3] also observed the production of solid polymer from *trans*-1,2-dichloroethylene but did not report the yield. Our polymer was a colourless powder, partly soluble in *NN*-dimethylformamide and in 1,1,2,2-tetrachloroethane but insoluble in most of the usual organic solvents. It softened above 240° and decomposed with charring above 290°. Weak infrared absorption at 1629 and 936 cm.$^{-1}$ showed the presence of

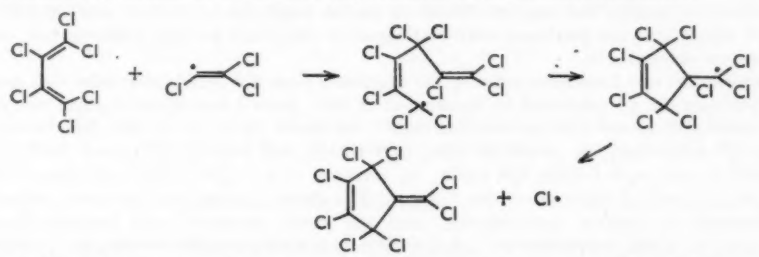
[7] Kitson, *Analyt. Chem.*, 1953, **25**, 1470.
[8] B.P. Specification C. 12,659/57, July 1958.

unsaturation (probably terminal CH:CHCl groups) and an *X*-ray powder photograph showed the absence of crystallinity.

The main product of γ-irradiation of trichloroethylene was a mixture of liquid and waxy oligomers with smaller quantities of hydrogen chloride, a crystalline solid, and explosive volatile material believed to be a mixture of mono- and di-chloroacetylenes. Newton [4] reported the production of these chloroacetylenes by α-radiolysis of trichloroethylene. Fractions corresponding closely to dimer and trimer were separated by distillation, and the physical constants of the dimer were in good agreement with those reported [2c] for the supposed 1,1,3,3,4,4-hexachlorobut-1-ene obtained by peroxide-initiated polymerisation of trichloroethylene. Analysis of the solid indicated a molecular formula $C_6H_4Cl_{10}$ (decachlorohexane) and its infrared spectrum confirmed the absence of unsaturation. In the larger-scale experiments the stabiliser (a nitrogen compound), present in the trichloroethylene, was not removed before irradiation; this had little effect on the yield of polymer, but the yield of hydrogen chloride decreased and chloroacetylenes were absent from the irradiated solution; during the early stages of irradiation, a crystalline, water-soluble solid, containing nitrogen and ionic chlorine, separated but this disappeared as the dose increased and it was not examined further.

Irradiation of tetrachloroethylene gave hexachloroethane, hexachlorobuta-1,3-diene, octachlorobut-1-ene (dimer), hexachloro-4-dichloromethylenecyclopentene,* and an oil of low volatility, probably consisting of higher oligomers.

Like Futrell and Newton,[3] we [5] consider the fission of a carbon–chlorine bond to be the principal radiolytic reaction in all the examples studied, and indeed this appears to be a feature of radiolysis in most halogen compounds.[9] The polymers, which are in all instances the main products, are then produced by a free-radical chain mechanism initiated by attack of a chlorine atom on a monomer molecule. The yields of polymer decrease, as expected, with increasing chlorine substitution, and *trans*-1,2-dichloroethylene gives a greater yield (including the solid) than the *cis*-compound. Futrell and Newton [3] also obtained greater total polymer yields from the *trans*-isomer but their *G* values are lower than in the present work because of the higher dose rate employed. In the case of tetrachloroethylene, where polymerisation is relatively least important, hexachlorobutadiene, the product of dimerisation of the initially formed trichlorovinyl radicals, can be readily isolated. Hexachloro-4-dichloromethylenecyclopentene may be a secondary product arising by attack of a trichlorovinyl radical on hexachlorobutadiene:



Futrell and Newton [3] consider that chloroacetylene and most of the hydrogen chloride, arising from the dichloroethylenes, are the products of "molecular" elimination of hydrogen chloride from an excited substrate molecule; this may also be true for the dichloroacetylene and hydrogen chloride produced from trichloroethylene. If this is the case, the action of traces of stabiliser (chemical nature unknown) in suppressing the yields of these compounds could be due to energy transfer from excited molecules of the olefin to the stabiliser.

* This compound was at first incorrectly identified [5] as octachlorocyclohexa-1,3-diene.

[9] Swallow, "Radiation Chemistry of Organic Compounds," Pergamon Press, London, 1960, p. 94.

Experimental

The radiation unit contained a ^{60}Co source (~100 c) and was similar in design and operation to that described by Gibson and Pierce.[10] Irradiations at the higher dose rates were carried out, by courtesy of Dr. W. Wild, inside a hollow cylindrical ^{60}Co source at the Atomic Energy Research Establishment, Harwell. Liquids were irradiated either (a) after degassing, in sealed evacuated glass ampoules (~40 ml. capacity) or (b) in cylindrical glass vessels of annular cross section enclosing the source. In the latter case, the vessels were fitted with ground-glass stoppers, but no other precautions were taken to exclude air. Dose rates quoted were determined by using the aqueous ferrous sulphate–sulphuric acid system [11] and are corrected for the greater electron density of the absorbing liquids. The G value for formation of ferric ion was taken as 15·5. Gas–liquid chromatography was carried out with apparatus of conventional design involving columns of kieselguhr (Johns-Manville Celite 545) impregnated with Silicone oil MS 550 (Hopkin and Williams).

Purification of Materials.—Commercial 1,2-dichloroethylene (May and Baker) was the source of both isomers, which were separated by fractional distillation and redistilled immediately before use. The purity of the two isomers was checked by gas–liquid chromatography; in the quantitative experiments the *trans*-isomer contained less than 0·5% of *cis*-compound, and the *cis*-isomer contained less than 0·1% of *trans*-compound; in the large-scale experiments each isomer contained less than 10% of the other. Trichloroethylene (Merck) was washed with 2N-hydrochloric acid, water, 2N-sodium carbonate, and water; after drying ($CaCl_2$) it was fractionated and redistilled immediately before use; for the large-scale experiments, no purification was carried out. Tetrachloroethylene (Merck or Hopkin and Williams) was washed with 2N-hydrochloric acid until no further yellow colour was produced in the aqueous layer, then with water, dried (P_2O_5), and distilled through a short column immediately before use.

Irradiation of 1,2-*Dichloroethylenes.*—*trans*-1,2-Dichloroethylene was degassed and sealed, under a vacuum, in glass ampoules which were irradiated for different times at a dose rate of $4{\cdot}36 \times 10^{17}$ ev ml.$^{-1}$ min.$^{-1}$. Hydrogen chloride was then estimated by treatment of an aliquot part with standard sodium hydroxide and back-titration. Solid polymer was removed by filtration, washed with ether, dried, and weighed. Monomer was then removed from the filtrate by distillation until the residue had constant weight. Irradiations were also performed, without degassing but after previous distillation of the samples under nitrogen, in an annular vessel (435 ml.) for different times at a dose rate of $0{\cdot}78 \times 10^{17}$ ev ml.$^{-1}$ min.$^{-1}$. In working-up of the larger irradiated samples, the final residue of oily polymers yielded a further small quantity of solid on addition of ether.

cis-1,2-Dichloroethylene was irradiated in sealed ampoules at a dose rate of $4{\cdot}36 \times 10^{17}$ ev ml.$^{-1}$ min.$^{-1}$ and the products were estimated as described for the *trans*-isomer; no solid polymer was produced.

Fractionation and Characterisation of the Oligomers from 1,2-*Dichloroethylenes.*—A sample of liquid polymer (53 g.) produced by irradiation of 90% *trans*-1,2-dichloroethylene was distilled under reduced pressure and yielded fractions: (*a*) dimer (7 g.), b. p. 82—84°/15 mm., n_D^{20} 1·5146, d_4^{20} 1·473 (lit.,[2c] b. p. 88°/20 mm., n_D^{20} 1·5150, d_4^{20} 1·473); (*b*) trimer (10·5 g.), b. p. 105—120°/2 mm., n_D^{20} 1·5392, d_4^{20} 1·559; (*c*) tetramer (6 g.), n_D^{20} 1·5493; (*d*) viscous oils and waxes (6 g.); and (*e*) charred residue (24 g.). The dimer, trimer, and tetramer were treated with bromine in carbon tetrachloride, and the solid products were recrystallised from acetic acid to yield, respectively: (*a*) 1,2-*dibromo*-1,3,4,4-*tetrachlorobutane*, m. p. 102—103° (Found: C, 14·0; H, 1·0; Hal, 84·9. $C_4H_4Br_2Cl_4$ requires C, 13·6; H, 1·1; Hal, 85·3%); liquid dibromide(s) were also produced; (*b*) 1,2-*dibromo*-1,3,4,5,6,6-*hexachlorohexane*, m. p. 121—124° (Found: C, 16·3; H, 1·4; Hal, 82·5. $C_6H_6Br_2Cl_6$ requires C, 16·0; H, 1·4; Hal, 82·6%); (*c*) 1,2-*dibromo*-1,3,4,5,6,7,8,8-*octachloro-octane*, m. p. 246—249° (Found: C, 18·0; H, 1·7; Hal, 80·5. $C_8H_8Br_2Cl_8$ requires C, 17·5; H, 1·5; Hal, 81·0%).

The polymer (164 g.) produced by irradiation of 90% *cis*-1,2-dichloroethylene yielded similar fractions in different proportions, as follows: (*a*) dimer (70 g.), b. p. 83—84°/15 mm., n_D^{20} 1·5155, d_4^{20} 1·474; (*b*) trimer (40 g.), b. p. 105—120°/2 mm., n_D^{20} 1·5388, d_4^{20} 1·558; (*c*)

[10] Gibson and Pierce, *Chem. and Ind.*, 1957, 613.
[11] Amphlett, *Discuss. Faraday Soc.*, 1952, **12**, 145.

XUM

tetramer (5 g.), n_D^{20} 1·5486; (*d*) viscous oils and waxes (10 g.); and (*e*) charred residue (39 g.). These oligomers yielded the same dibromides as were obtained from the *trans*-isomer.

Chromatography of the Tetrachlorobutene Fraction.—The dimer (1 ml.) was chromatographed at 130° in nitrogen (300 ml. min.$^{-1}$) on a column (8 ft. × 1 in.) packed with firebrick (40—60 mesh) impregnated with tritolyl phosphate (30% w/w of packing). Passage of the effluent through a U-tube at −78° yielded, after 250 min., cis-1,3,4,4-*tetrachlorobut*-1-*ene*, b. p. 193—195°/760 mm., n_D^{20} 1·5132 after redistillation (Found: C, 25·8; H, 2·0; Cl, 72·2. $C_4H_4Cl_4$ requires C, 24·8; H, 2·1; Cl, 73·1%) and, after 310 min., the trans-*isomer*, b. p. 197—198°/760 mm., n_D^{20} 1·5198 after redistillation (Found: C, 25·8; H, 2·2; Cl, 71·8%). When a shorter column was used, separation was less efficient but later fractions contained a substance with infrared absorption at 855 cm.$^{-1}$.

Irradiation of Trichloroethylene.—Trichloroethylene (3857 g.), with stabiliser present, was irradiated for 358 hr. (total dose approximately 8 × 10^{23} ev). After 24 hr., needle-shaped crystals filled the vessel but only a trace of solid (A) remained when irradiation ceased. Removal of monomer by distillation afforded a dark-brown viscous oil (64 g.) containing a solid (B). A portion of the oil (43 g.), after removal of solid (4·1 g.) by dilution with ethanol and filtration, yielded on distillation fractions: (*a*) slightly impure dimer (12 g.), b. p. 41°/0·01 mm., n_D^{20} 1·5440, d_4^{20} 1·674 (lit.,[2c] n_D^{20} 1·5461, d_4^{20} 1·676), giving no reaction with bromine; (*b*) orange oils (14·5 g.) which could not be further purified; and (*c*) charred residue (12·4 g.). Solid (A), needles, m. p. 224—229°, contained nitrogen and ionic chlorine. Solid (B) formed plates, m. p. 216—217°, from chloroform (Found: C, 16·7; H, 1·0; Cl, 82·1%; *M*, 430. Calc. for $C_6H_4Cl_{10}$: C, 16·7; H, 0·94; Cl, 82·3%; *M*, 431). Trichloroethylene (free from stabiliser) was also irradiated in sealed evacuated ampoules (dose rate, 4·88 × 10^{17} ev ml.$^{-1}$ min.$^{-1}$) as described for the dichloroethylenes. During distillation, a vigorous evolution of gas occurred at 20—40°, culminating in a flash and deposition of carbon in the Vigreux column; this is attributed to the presence of mono- and di-chloroacetylenes. After removal of monomer by distillation, the residual oil was separated from the solid (B) by dilution with ethanol, filtration, and evaporation of the ethanol. The residue, which possibly still contained a little of compound (B) in solution, was weighed. Similar experiments were carried out with stabiliser present.

Irradiation of Tetrachloroethylene.—Tetrachloroethylene (393 ml.) was irradiated for 232 hr. (total dose 48 × 10^{22} ev). Removal of monomer by distillation then afforded a red, viscous oil (12 g.); hexachloroethane (0·3 g.), m. p. and mixed m. p. 185—186°, solidified in the condenser. Distillation of the oil provided the fractions: (*a*) hexachloroethane (0·1 g.); (*b*) hexachlorobuta-1,3-diene (2 g.), b. p. 60—80° (bath temp.)/0·01 mm., ultraviolet and infrared spectra identical with those of an authentic specimen; (*c*) hexachloro-4-dichloromethylenecyclopentene (0·4 g.), prisms (from benzene), m. p. and mixed m. p. 182—183°, infrared and ultraviolet spectra identical with those of an authentic specimen;[12] (*d*) *octachlorobut*-1-*ene* (3 g.), b. p. 100—120° (bath temp.)/10^{-4} mm., n_D^{20} 1·5844, $\nu_{max.}$ 1642 cm.$^{-1}$ (Found: C, 14·3; Cl, 85·3%; *M*, 335. C_4Cl_8 requires C, 14·5; Cl, 85·5%; *M*, 332); and (*e*) a red, very viscous oil (5 g.), b. p. 140—180° (bath temp.)/10^{-4} mm.

We thank the United Kingdom Atomic Energy Authority, Research Group, Harwell, for financial support, including provision of research assistantships (to W. M., W. H. T., and A. H. M.).

CHEMISTRY DEPARTMENT, UNIVERSITY OF EDINBURGH. [*Received, May 1st*, 1961.]

[12] McBee, Ungnade, Rakoff, and Dinbergs, *J. Amer. Chem. Soc.*, 1955, **77**, 4379.

XUM

885. *Pyrone Series. Part IV.*[1] *5-Aryloxy-2-pyrones. The Corresponding 2-Thiopyrones, Pyridones, 1-Hydroxy- and 1-Amino-2-pyridones, and Related 4,5,6-Triphenyl-2-pyrones.*

By Ibrahim El-Sayed El-Kholy, Fathi Kamel Rafla, and Gabra Soliman.

Some 5-aryloxy-2-pyrones have been prepared and their structures determined by alkaline fission. These and 4,5,6-triphenyl-2-pyrone have been converted into 2-thiopyrones, 2-pyridones, 1-methyl-2-pyridones, and 1-amino-2-pyridones. The last three types have been inter-related, and 2-alkoxypyridines have been formed from the 2-pyridones. 1-Hydroxy-2-pyridones have been prepared by the action of hydroxylamine on the pyrones in pyridine. The structures of these compounds are apparent from their infrared and ultraviolet spectra, which are recorded.

In earlier papers[1,2] of this series, we showed that ethyl phenylpropiolate undergoes Michael addition with deoxybenzoins and ω-methoxyacetophenones, giving the corresponding 2-pyrones. We now report that ω-aryloxyacetophenones (I; R = OAr) condense with this acetylenic ester, giving 5-aryloxy-4,6-diphenyl-2-pyrones (II; R = OAr). In distinction from a former series,[2] these aryloxypyrones were not accompanied by the *trans*-isomers of the hypothetical intermediate adducts. Their 2-pyrone structure was determined by fission to *cis*-4-aryloxy-5-oxo-3,5-diphenylpentenoic acids (III; R = OAr) whose esters (IV) were readily cyclised to the pyrones.

Having in our hands three types of trisubstituted 2-pyrones, we have studied the infrared absorption spectra of representative members (II; R = Ph, OMe, or OPh) (see Table 1). Bands in the 1718—1724 cm.$^{-1}$ region are attributable to the 2-pyrone carbonyl stretching frequency, whereas the 1613—1634 and 1577—1592 cm.$^{-1}$ maxima are due to the carbon–carbon double-bond stretching frequencies which characterise the 2-pyrone structure.[3,4] The bands at 1471—1497 and 1441—1458 cm.$^{-1}$ appear to signify the presence of phenyl groups[5a] in these pyrones and other compounds in Table 1.

Like 4,6-diaryl-5-methoxy-2-pyrones,[1] the 5-aryloxy-4,6-diphenyl-2-pyrones as well as 4,5,6-triphenyl-2-pyrone were readily converted by our usual technique into the corresponding 2-thiopyrones (V) in quantitative yield. These are characterised by strong absorption in the range 1109—1111 cm.$^{-1}$ (Table 1) which is attributable to the C=S stretching frequency.[6]

These 2-thiopyrones are converted into the pyrones by hydrogen peroxide in glacial acetic acid, but not by semicarbazide and they are resinified by hydroxylamine or hydrazine hydrate.[1] 4,5,6-Triphenyl-2-thiopyrone reacted with hydroxylamine in a neutral medium and with hydrazine hydrate, giving 1-hydroxy-4,5,6-triphenyl-2-pyridone oxime (VI; R = Ph) and 1-amino-4,5,6-triphenyl-2-thiopyridone (VII; R = Ph), respectively.

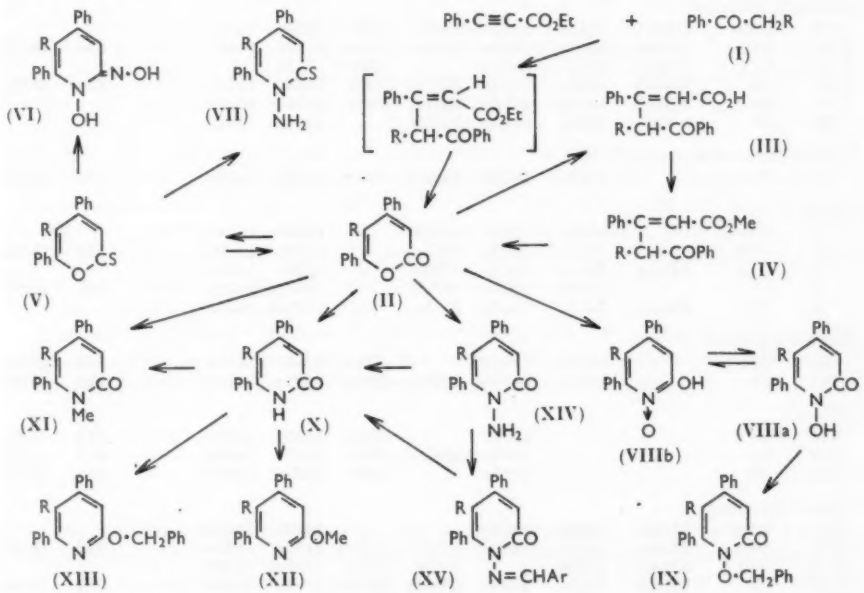
5-Methoxy-4,6-diphenyl-2-pyrone (II; R = OMe) was previously shown to react slowly with hydroxylamine in a neutral medium, giving 1-hydroxy-4,6-diphenyl-5-methoxy-2-pyridone (VIII; R = OMe) whereas its thio-analogue (V; R = OMe) was converted into the pyrone. In this paper, however, we report that this pyrone, 5-methoxy-4-phenyl-6-*p*-tolyl-2-pyrone,[1] 5-phenoxy-4,6-diphenyl-2-pyrone, and 4,5,6-triphenyl-2-pyrone give the corresponding 1-hydroxy-2-pyridones (VIIIa or b) on reaction with hydroxylamine in pyridine.

[1] Part III, El-Kholy, Rafla, and Soliman, *J.*, 1959, 2588.
[2] Soliman and El-Kholy, *J.*, 1955, 2911.
[3] Wiley and Slaymaker, *J. Amer. Chem. Soc.*, 1956, **78**, 2393.
[4] Wiley and Esterle, *J. Org. Chem.*, 1957, **22**, 1257.
[5] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1959, pp. (*a*) 69, (*b*) 96, (*c*) 267, (*d*) 205.
[6] Spinner, *J. Org. Chem.*, 1958, **23**, 2037; *J.*, 1960, 1237.

XUM

Though these compounds give an intense red colour with ferric chloride, the structure (VIIIa) is preferably assigned to them as they show strong carbonyl absorption at 1650 (±5) cm.$^{-1}$, indicating that *N*-hydroxy-substitution does not affect the characteristic 2-pyridone carbonyl band. The broad band in the region 3030—3145 cm.$^{-1}$ is probably associated with the tautomerism (VIIIa ⟷ b) or strong chelated intramolecular hydrogen bonding in the solid state as well as in solution.[5b] Further, the 1-benzyloxy-ether (IX; R = Ph) obtained by the action of benzyl chloride on 1-hydroxy-4,5,6-triphenyl-2-pyridone in alkali is not susceptible to hydrolysis with hydrochloric acid and shows carbonyl absorption at 1664 cm.$^{-1}$, but the broad absorption in the region 3030—3145 cm.$^{-1}$ is lacking. This conclusion is supported by the ultraviolet absorption maxima recorded in Table 1 which are within the range of other 1-hydroxy-2-pyridones studied by Cunningham *et al.*,[7] Shaw,[8] Adams and Miyano,[9] Wiley and Slaymaker,[3] and Gardner and Katritzky.[10]

Similarly, 1-hydroxy-4,5,6-triphenyl-2-pyridone oxime (VI; R = Ph) has an analogous structure since it is characterised by strong absorption at 1639 cm.$^{-1}$ due to the C=N stretching frequency.[5c]



A new series of 2-pyridones (X) and 1-methyl-2-pyridones (XI) has been obtained from these 5-aryloxy-4,6-diphenyl-2-pyrones and 4,5,6-triphenyl-2-pyrone by the action of ammonia and methylamine, respectively. These pyridones, however, behave as tautomeric systems as they display a red colour with ferric chloride. Accordingly, they yielded 1-methyl-2-pyridones (XI) with methyl iodide and alkali, and 2-methoxypyridines (XII) on treatment with diazomethane in ether–methanol or by the action of methyl iodide on the silver salt. On the other hand, formation of 2-benzyloxy-4,5,6-triphenylpyridine (XIII; R = Ph) by the action of benzyl chloride on the potassium or the silver salt of 4,5,6-triphenyl-2-pyridone is at variance with the general mode of alkylation.[11a]

[7] Cunningham, Newbold, Spring, and Stark, *J.*, 1949, 2091.
[8] Shaw, *J. Amer. Chem. Soc.*, 1949, **71**, 67; Shaw and Lott, *ibid.*, p. 70.
[9] Adams and Miyano, *J. Amer. Chem. Soc.*, 1954, **76**, 3168.
[10] Gardner and Katritzky, *J.*, 1957, 4375.
[11] Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley, Inc., New York, 1950, pp. (*a*) 534, (*b*) 436.

TABLE 1.

Infrared and ultraviolet spectra.

[Infrared spectra ($cm.^{-1}$) of the methoxy-series were measured on a Perkin–Elmer 21 spectrophotometer for a KBr disc. The other compounds were measured with a Perkin–Elmer 137 spectrophotometer for a KBr disc. For solution spectra the thickness was 0·5 mm. Ultraviolet spectra are for ethanol solutions.]

Formula	R	OH or NH stretching	C=O	C=C		*N*-Substn.	Ph group		C=S	U.V. peak (mμ)	(log ε)
2-Pyrones											
II	OMe		1718s	1621s	1577w	—	1490s	1445s	—		
II	OPh		1724s	1634w	1592w	—	1493s	1449m	—		
II	Ph		1721s	1613m	1577w	—	1490s	1449s	—		
2-Thiopyrones											
V	OMe		—	1608s	1572w	—	1497s	1443s	1109s		
V	OPh		—	1618s	1597w	—	1490s	1447s	1111s		
V	Ph		—	1616s	1587m	—	1488s	1445s	1111s		
1-Hydroxy-2-pyridones											
VIII	OMe	3030sb	1645s	1603w	1575w	1553s	1488s	1453s	—		
VIII	OPh	3125sb	1655s	1600w	1585m	1555s	1493s	1458s	—	340	(3·88)
VIII	OPh †	3040sb	1650s	1590w		1538s	1471s		—		
VIII	Ph	3145sb	1655s	1610w	1587m	1531s	1493s	1449s	—	328	(3·83)
VIII	Ph †	3040sb	1647s	1613w	1587w	1531s	1493w	1445w	—		
IX	Ph	—	1664s	1660w	1582w		1481s	1441s	—		
1-Hydroxy-2-pyridone oxime											
VI	Ph		1639s *	1613w	1590w	1555m	1486w	1449s	—	335	(3·76)
2-Pyridones											
X	OMe		1642s	1595s	1575w	—	1490m	1449m	—		
X	OPh		1645s	1600w	1587s	—	1488s	1449s	—	338	(3·94)
X	OPh †	3400m	1650s	1613s	1590s	—	1490s	1449m	—		
X	Ph		1647s	1600w	1572w	—	1493m	1451s	—	330	(3·94)
X	Ph †	3448m	1653s	1605m	1575w	—	1497m	1453m	—		
1-Methyl-2-pyridones											
XI	OPh		1653s	1613w		1515w	1481s	1441w	—	335	(3·85)
XI	Ph		1661s	1608w	1587s	1520m	1493s	1449w	—	325	(3·87)
Pyridines											
XII	OPh		—	1597s		1555s	1493s	1458s	—	312	(3·94)
XII	Ph		—	1597s	1580s	1555s	1497w	1449w	—	305	(3·87)
XIII	Ph		—	1587s		1563s	1493m	1441s	—	308	(4·49)
1-Amino-2-pyridones											
XIV	OMe	3226m	1656s	1608w			1486s	1445m	—		
XIV	OPh	3226m	1658s	1600w	1575w	1558m	1486s	1443w	—	342	(3·88)
XIV	OPh †	3344m	1653s		1575s	1538s	1481m	1443w	—		
XIV	Ph	3215m	1650s	1600w	1580m	1546m	1484s	1443m	—	332	(3·94)
XIV	Ph †	3400m	1650s	1600w	1582m	1543m	1484m	1441m	—		
1-Amino-2-thiopyridone											
VII	Ph	3125m	—	1595s	1577s	1515m	1493s	1449s	1099s		

w = weak; m = medium; s = strong; b = broad.

* C=N stretching frequency. † In $CHCl_3$.

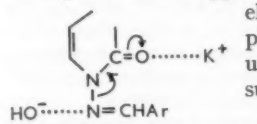
Analogously to 2-pyridone [12] which exists predominantly as an amide in the solid state, the polysubstituted 2-pyridones (X) and their *N*-methyl derivatives (XI) are characterised by strong absorption in the region 1661—1642 $cm.^{-1}$ associated with the pyridone carbonyl, and the bands 1613—1595 and 1590—1572 $cm.^{-1}$ are attributed to carbon–carbon double bonds. The broad bands in the region 3—4 μ shown by the pyridones (X) signify N–H · · · O hydrogen bonding in the solid state, whereas the sharp band at 3448, 3400 $cm.^{-1}$ shown by 4,5,6-triphenyl-2-pyridone and 5-phenoxy-4,6-diphenyl-2-pyridone, respectively,

[12] Mason, *J.*, 1957, 4874.

Vol. 1961, page 4492. Table 1, line 11 *. *For* (4·49) *read* (4·09).

in chloroform is characteristic of NH stretching frequency.[5d] Conversely, the 2-methoxypyridines (XII) and 2-benzyloxy-4,5,6-triphenylpyridine (XIII; R = Ph) do not show carbonyl absorption, and their ultraviolet maxima at 305—312 mμ (log ε 3·87—3·94) are shorter than the corresponding maxima (325—338 mμ, log ε 3·85—3·94) of the isomeric 1-methyl-2-pyridones.[11b]

1-Amino-2-pyridones have been prepared by the action of hydrazine hydrate on 5-aryloxy-2-pyrones and 4,5,6-triphenyl-2-pyrone, as well as on methyl *cis*-4-aryloxy-5-oxo-3,5-diphenylpentenoate (IV; R = OAr) and *cis*-5-oxo-3,4,5-triphenylpentenoate (IV; R = Ph) and related esters. These aminopyridones are characterised by conversion into the pyridones by nitrous acid, diacylation, and formation of arylidene derivatives. Further, the diacylamines are susceptible to stepwise hydrolysis; the arylideneaminopyridones are hydrolysed by concentrated alkali to the pyridone and the corresponding aromatic acid. In response to the approach of the cationic reagent, the =N·N·C=O group appears to be electron-releasing and simultaneously fission of the N–N link takes place with the formation of an aldoxime. The latter appears to undergo elimination of water, giving rise to a nitrile which is susceptible to hydrolysis.



The pyridone structure of these amines (XIV) is evident from their infrared and ultraviolet absorption data (Table 1) which are analogous to those of similarly constituted 1-amino-2-pyridones reported by other workers.[3,13]

Besides the characteristic carbonyl absorption at 1650—1658 cm.$^{-1}$, the 1-aminopyridones, like 1-methyl-2-pyridones and 1-hydroxy-2-pyridones, exhibit absorption at 1515—1558 cm.$^{-1}$ attributable to *N*-substitution (6·47—6·54 μ).[3,13] Further, their chloroform solutions show a medium (3400 cm.$^{-1}$) and a weak band (3280 cm.$^{-1}$) indicating the free amino-group.[5d] In the solid state, however, there is a band at 3226 cm.$^{-1}$. Moreover, the absence of broad absorption in the region 3—4 μ for 1-amino-2-pyridones and 1-methyl-2-pyridones supports the previous views regarding hydrogen bonding in solid *N*-unsubstituted 2-pyridones.

However, 1-amino-4,5,6-triphenyl-2-thiopyridone (VII; R = Ph) is characterised by strong absorption at 1100 cm.$^{-1}$ attributable to the C=S group, but owing to the scarcity of the material, chemical evidence of its structure has not been sought.

Experimental

Light petroleum had b. p. 50—70°.

5-Phenoxy-4,6-diphenyl-2-pyrone.—ω-Phenoxyacetophenone [14] (4·2 g., 1 mol.) and ethyl phenylpropiolate (3·5 g., 1 mol.) were added to an ice-cold suspension of sodium ethoxide (1·4 g., 1 mol.) in ether, and the mixture was kept in the ice-chest for 2 days, then mixed with water. The ethereal solution yielded an oily residue (5·7 g.) from which the pyrone (1·4 g.), m. p. 128°, crystallised. It recrystallised from methanol in yellowish-white prismatic needles, m. p. 131° (Found: C, 81·1; H, 4·7. $C_{23}H_{16}O_3$ requires C, 81·2; H, 4·7%). The alkaline layer yielded phenylpropiolic acid (0·8 g.). This pyrone was recovered unchanged after 8 hr. in boiling ethanol with semicarbazide or hydroxylamine.

cis-*5-Oxo-4-phenoxy-3,5-diphenylpentenoic Acid.*—The foregoing pyrone (1·5 g.) was warmed with 3% methanolic potassium hydroxide (30 ml.), and the solution was diluted with water and extracted with ether. The alkaline solution gave, on acidification and extraction with ether, a yellow oil (1·5 g.) from which the *pentenoic acid* was obtained on treatment with light petroleum. It crystallised from dilute methanol in prisms, m. p. 159° (decomp.) (Found: C, 77·1; H, 5·2. $C_{23}H_{18}O_4$ requires C, 77·1; H, 5·1%).

The *methyl ester* was prepared by refluxing a methanol solution of the acid (0·2 g.) containing a few drops of concentrated hydrochloric acid or by the action of ethereal diazomethane. It

[13] Hoegerle, *Helv. Chim. Acta*, 1958, **41**, 539.
[14] Davies and Middleton, *J.*, 1958, 822.

crystallised from methanol in prismatic needles, m. p. 101° (Found: C, 77·1; H, 5·5; OMe, 8·2. $C_{24}H_{20}O_4$ requires C, 77·3; H, 5·4; OMe, 8·3%). It was converted into the pyrone when its ethereal solution was kept with sodium ethoxide at 0° for 4 hr.

4,6-*Diphenyl*-5-p-*tolyloxy*-2-*pyrone* was prepared as above but from ω-*p*-tolyloxyacetophenone,[14] in 25% yield, and crystallised from benzene in yellow elongated prisms, m. p. 162° (Found: C, 81·05; H, 5·0. $C_{24}H_{18}O_3$ requires C, 81·3; H, 5·1%).

cis-5-*Oxo*-3,5-*diphenyl*-4-p-*tolyloxypentenoic acid* was prepared by alkaline fission of the pyrone and crystallised from benzene–light petroleum in prisms, m. p. 155° (decomp.) (Found: C, 77·5; H, 5·4. $C_{24}H_{20}O_4$ requires C, 77·5; H, 5·4%). Its *methyl ester* crystallised from methanol in prisms, m. p. 94° (Found: C, 77·5; H, 5·7; OMe, 7·9. $C_{25}H_{22}O_4$ requires C, 77·7; H, 5·7; OMe, 8·0%).

5-p-*Chlorophenoxy*-4,6-*diphenyl*-2-*pyrone*.—ω-*p*-Chlorophenoxyacetophenone,[15] prepared in 88% yield by refluxing *p*-chlorophenol (15·5 g., 1·2 mol.), phenacyl bromide (20 g., 1 mol.), and potassium carbonate (14 g.) in acetone for 4 hr., crystallised from ethanol in plates, m. p. 101° (Found: C, 68·3; H, 4·55; Cl, 14·3. Calc. for $C_{14}H_{11}ClO_2$: C, 68·3; H, 4·5; Cl, 14·4%). Its *oxime* crystallised from benzene–light petroleum in prismatic plates, m. p. 124° (Found: N, 5·0. $C_{14}H_{12}ClNO_2$ requires N, 5·35%). The *pyrone* was prepared in 25% yield from this ketone in benzene and crystallised from benzene–light petroleum in pale yellow needles, m. p. 162° (Found: C, 73·6; H, 4·1; Cl, 9·2. $C_{23}H_{15}ClO_3$ requires C, 73·7; H, 4·0; Cl, 9·5%).

cis-4-p-*Chlorophenoxy*-5-*oxo*-3,5-*diphenylpentenoic acid* crystallised from benzene–light petroleum in needles, m. p. 162° (decomp.) (Found: C, 70·8; H, 4·5; Cl, 8·7. $C_{23}H_{17}ClO_4$ requires C, 70·3; H, 4·4; Cl, 9·1%). Its *methyl ester* crystallised from light petroleum (b. p. 30—50°) in needles, m. p. 104—105° (Found: C, 70·75; H, 4·95; OMe, 7·5. $C_{24}H_{19}ClO_4$ requires C, 70·8; H, 4·7; OMe, 7·6%).

5-p-*Bromophenoxy*-4,6-*diphenyl*-2-*pyrone*.—ω-p-*Bromophenoxyacetophenone* was prepared in 83% yield from *p*-bromophenol and phenacyl bromide as above and crystallised from ethanol in elongated plates, m. p. 108° (Found: C, 57·4; H, 3·9; Br, 27·5. $C_{14}H_{11}BrO_2$ requires C, 57·7; H, 3·8; Br, 27·5%). Its *semicarbazone* crystallised from ethanol in plates, m. p. 183° (Found: C, 51·4; H, 4·1; N, 11·8; Br, 23·0. $C_{15}H_{14}BrN_3O_2$ requires C, 51·7; H, 4·05; N, 12·1; Br, 23·0%). The *pyrone* was prepared in 26% yield from this ketone in benzene and crystallised from benzene in yellow platelets, m. p. 177° (Found: C, 65·6; H, 3·6; Br, 19·0. $C_{23}H_{15}BrO_3$ requires C, 65·9; H, 3·6; Br, 19·1%).

cis-4-p-*Bromophenoxy*-5-*oxo*-3,5-*diphenylpentenoic acid* crystallised from benzene–light petroleum in needles, m. p. 174° (decomp.) (Found: C, 63·6; H, 3·9; Br, 17·8. $C_{23}H_{17}BrO_4$ requires C, 63·2; H, 3·9; Br, 18·3%). Its *methyl ester* crystallised from light petroleum in needles, m. p. 111° (Found: C, 63·8; H, 4·3; OMe, 6·7. $C_{24}H_{19}BrO_4$ requires C, 63·9; H, 4·2; OMe, 6·8%).

5-p-*Iodophenoxy*-4,6-*diphenyl*-2-*pyrone*.—ω-*p*-Iodophenoxyacetophenone was prepared in 85% yield from *p*-iodophenol and phenacyl bromide and crystallised from ethanol in elongated prisms, m. p. 108° (Found: C, 50·2; H, 3·5; I, 36·8. $C_{14}H_{11}IO_2$ requires C, 49·7; H, 3·3; I, 37·5%). Its *oxime* crystallised from methanol in elongated plates, m. p. 131° (Found: N, 3·7. $C_{14}H_{12}INO_2$ requires N, 4·0%). The *pyrone* was prepared in 24% yield from this ketone in benzene and crystallised from benzene in yellow prisms, m. p. 210° (Found: C, 58·75; H, 3·4; I, 28·05. $C_{23}H_{15}IO_3$ requires C, 59·2; H, 3·2; I, 27·2%).

6-p-*Methoxyphenyl*-5-*phenoxy*-4-*phenyl*-2-*pyrone*.—4-Methoxy-ω-phenoxyacetophenone,[16] m. p. 67°, was prepared in 65% yield by condensation of phenol with ω-bromo-*p*-methoxyacetophenone as above and was freed from 1,2-di-*p*-methoxybenzoylethane [17] by crystallisation from ethanol. The *pyrone* was prepared in 26% yield from the former ketone in ether and crystallised from benzene in yellow needles, m. p. 179° (Found: C, 77·85; H, 5·0. $C_{24}H_{18}O_4$ requires C, 77·8; H, 4·9%).

cis-5-p-*Methoxyphenyl*-5-*oxo*-4-*phenoxy*-3-*phenylpentenoic acid* crystallised from benzene–light petroleum in prisms, m. p. 169° (decomp.) (Found: C, 74·6; H, 5·3. $C_{24}H_{20}O_5$ requires C, 74·2; H, 5·2%).

The 2-*thiopyrones* of Table 2 were prepared by heating the pyrones with phosphorus pentasulphide in toluene for 3—4 hr. and recovered from the medium after washing with ammonium sulphide; they crystallised from benzene–light petroleum.

[15] Wright and Lincoln, *J. Amer. Chem. Soc.*, 1952, **74**, 6301.
[16] Stoermer and Atenstädt, *Ber.*, 1902, **35**, 3565.
[17] Holleman, *Rec. Trav. chim.*, 1891, **10**, 216.

TABLE 2.

2-Thiopyrones (V).

R	M. p.	Form *	Found (%) C	H	S	Formula	Required (%) C	H	S
C_6H_5·O	192°	Prisms	77·85	4·5	8·9	$C_{23}H_{16}O_2S$	77·5	4·5	9·0
p-Me·C_6H_4·O	143	Prisms	77·9	4·8	8·7	$C_{24}H_{18}O_2S$	77·8	4·9	8·7
p-Cl·C_6H_4·O	177	Needles	70·6	3·8	8·2	$C_{23}H_{15}ClO_2S$	70·65	3·9	8·2
p-Br·C_6H_4·O	180	Needles	63·5	3·2	7·3	$C_{23}H_{15}BrO_2S$	63·45	3·5	7·4
C_6H_5	218	Needles	80·7	4·8	9·5	$C_{23}H_{16}OS$	81·1	4·7	9·4
6-*p*-MeO·C_6H_4·5-PhO-4-Ph	185	Needles	74·45	4·7	8·3	$C_{24}H_{18}O_3S$	74·6	4·7	8·3

* All orange-red, except the first which was red.

Action of Hydrogen Peroxide on the 2-Thiopyrones.—When a warm solution of the 2-thiopyrone (0·5 g.) in glacial acetic acid (10 ml.) was treated with 1 ml. of hydrogen peroxide (100-vol.), the initial dark red colour suddenly changed to pale yellow and, on dilution, the corresponding 2-pyrone crystallised.

These 2-thiopyrones were recovered unchanged after being heated with semicarbazide in methanol for 10 hr. and, except when R = Ph, resinous products were obtained from them by the action of hydroxylamine or hydrazine hydrate.

1-*Hydroxy*-4,5,6-*triphenyl*-2-*pyridone Oxime.*—A solution of 4,5,6-triphenyl-2-thiopyrone (0·3 g.) in ethanol (45 ml.) was refluxed with hydroxylamine hydrochloride (0·3 g.) and sodium acetate (0·3 g.) in 2 ml. of water for 4 hr. The *pyridone oxime* (0·3 g.), recovered by concentration and dilution, crystallised from pyridine–methanol in yellow prisms, m. p. 203° (decomp.) (Found: C, 77·8; H, 5·3; N, 8·4. $C_{23}H_{18}N_2O_2$ requires C, 77·9; H, 5·1; N, 7·9%). This gave a green colour with ferric chloride, reduced copper acetate solution and Tollens's reagent, and was recovered unchanged after being heated with hydrochloric acid.

1-*Amino*-4,5,6-*triphenyl*-2-*thiopyridone.*—A mixture of 4,5,6-triphenyl-2-thiopyrone (0·6 g.) and 85% hydrazine hydrate (2·5 ml.) in ethanol (20 ml.) was refluxed for 5 hr. The thiopyrone gradually passed into solution and the mixture became yellow. After dilution and cooling, the 1-*amino-compound* (0·1 g.) separated and crystallised from methanol in yellow plates, m. p. 195° (Found: C, 78·3; H, 5·0; N, 7·9; S, 9·1. $C_{23}H_{18}N_2S$ requires C, 77·9; H, 5·1; N, 7·9; S, 9·05%). It gave with ferric chloride a reddish-brown colour which gradually faded, and it reduced Fehling's solution and Tollens's reagent.

The 2-*pyridones* (X) recorded in Table 3 were prepared in quantitative yield by heating the corresponding pyrones (about 0·7 g.) in sealed tubes with 25% aqueous ammonia (4 ml.) for 3—4 hr. at temperatures within the range of their m. p. These pyridones crystallised from pyridine (P)–methanol (M), benzene (B), or glacial acetic acid (G) in needles, which gave an orange-red colour with ferric chloride and a negative test with titanium trichloride.

TABLE 3.

2-Pyridones (X).

R	M. p.	Solvent	Found (%) C	H	N	Hal	Formula	Required (%) C	H	N	Hal
C_6H_5·O	233°	P–M	81·4	5·0	4·2	—	$C_{23}H_{17}NO_2$	81·4	5·05	4·1	—
p-Me·C_6H_4·O ...	252	P–M	81·5	5·1	4·0	—	$C_{24}H_{19}NO_2$	81·55	5·4	4·0	—
p-Cl·C_6H_4·O ...	241	P–M	73·4	4·1	3·9	9·5	$C_{23}H_{16}ClNO_2$	73·9	4·3	3·75	9·5
p-Br·C_6H_4·O ...	247	P–M	66·2	4·0	3·5	18·6	$C_{23}H_{16}BrNO_2$	66·0	3·9	3·35	19·1
C_6H_5	277	B	85·4	5·2	4·6	—	$C_{23}H_{17}NO$	85·4	5·3	4·3	—

The 1-*methyl*-2-*pyridones* listed in Table 4 of the above-mentioned pyridones were prepared by heating the respective pyrones (about 0·7 g.) with 33% aqueous methylamine in sealed tubes for 3 hr. at 180—190°. They were also prepared by heating the pyridones (about 0·2 g.) with methyl iodide (4 ml.) for 3 hr. at 180—190°. The 1-methyl-2-pyridones crystallised from dilute methanol or benzene–light petroleum (L) and were characterised by giving a brown colour with ferric chloride.

2-*Methoxy*-5-p-*phenoxy*-4,6-*diphenylpyridine* (XII; R = OPh).—The dry silver salt of 5-phenoxy-4,6-diphenyl-2-pyridone, prepared by addition of a 66% solution of aqueous silver nitrate (5 ml.) to a solution of the pyridone (0·7 g.) in 5·5% methanolic potassium hydroxide

(20 ml.), was refluxed with methyl iodide for 4 hr. After filtration of silver iodide, the *methoxypyridine* (0·7 g.) was recovered from the filtrate and crystallised from ethanol in needles, m. p. 107—108°, which gave a negative ferric chloride test (Found: C, 81·6; H, 5·4; N, 4·15; OMe, 8·9. $C_{24}H_{19}NO_2$ requires C, 81·55; H, 5·4; N, 4·0; OMe, 8·8%). This pyridine was also obtained by the action of diazomethane on the pyridone in ether–methanol.

TABLE 4.

1-Methyl-2-pyridones (XI).

R	M. p.	Appearance	Solvent	Found (%) C	H	N	Formula	Required (%) C	H	N
C_6H_5·O	167°	Needles	M	81·6	5·5	4·0	$C_{24}H_{19}NO_2$	81·55	5·4	4·0
p-Me·C_6H_4·O ...	180	Yellow needles	M	81·6	5·65	3·7	$C_{25}H_{21}NO_2$	81·7	5·8	3·8
p-Cl·C_6H_4·O	200	Needles	M	74·7	4·7	3·6	$C_{24}H_{18}ClNO_2$ [a]	74·3	4·7	3·6
p-Br·C_6H_4·O	209	Prisms	B–L	67·2	4·2	3·0	$C_{24}H_{18}BrNO_2$ [b]	66·7	4·2	3·2
C_6H_5	189	Needles	M	85·7	5·5	4·0	$C_{24}H_{19}NO$	85·4	5·7	4·15

[a] Cl: Found, 8·55. Reqd., 9·1%. [b] Br: Found, 19·1. Reqd., 18·5%.

2-*Methoxy*-4,5,6-*triphenylpyridine* (XII; R = Ph) was prepared from the dry silver salt of 4,5,6-triphenyl-2-pyridone and crystallised from ethanol in needles, m. p. 144—145° (Found: C, 85·3; H, 5·4; N, 4·3; OMe, 9·4. $C_{24}H_{19}NO$ requires C, 85·4; H, 5·7; N, 4·15; OMe, 9·2%). The ethanolic mother liquor yielded traces of 1-methyl-4,5,6-triphenyl-2-pyridone, m. p. and mixed m. p. 188—189°. The action of diazomethane on this pyridone in ether–methanol gave only the 2-methoxypyridine.

Other Alkylations.—(a) A mixture of 4,5,6-triphenyl-2-pyridone (0·3 g.), potassium hydroxide (0·7 g.), and methyl iodide (20 ml.) was refluxed for 2 hr. and filtered. When the residue recovered by evaporation of the filtrate was dissolved in hot methanol, 2-methoxy-4,5,6-triphenylpyridine (0·07 g.), m. p. 144—145°, crystallised. The mother liquor yielded, on dilution, 1-methyl-4,5,6-triphenyl-2-pyridone (0·2 g.) which crystallised from dilute methanol in needles, m. p. and mixed m. p. 189°.

(b) 2-*Benzyloxy*-4,5,6-*triphenylpyridine* (XIII; R = Ph) was obtained when a solution of 4,5,6-triphenyl-2-pyridone (0·3 g.) in absolute ethanol (20 ml.) containing sodium ethoxide (0·3 g. of sodium) was refluxed with benzyl chloride (1·7 g.) for 2 hr. When the filtrate was diluted with water, the benzyloxypyridine (0·2 g.) was recovered and crystallised from methanol in needles, m. p. 150°, which gave a negative ferric chloride test (Found: C, 87·0; H, 5·5; N, 3·7. $C_{30}H_{23}NO$ requires C, 87·1; H, 5·6; N, 3·4%). It was also prepared in 70% yield when the silver salt of 4,5,6-triphenyl-2-pyridone (0·9 g.) was refluxed with benzyl chloride (3 g.) in dry benzene for 3 hr.

1-*Hydroxy*-5-*phenoxy*-4,6-*diphenyl*-2-*pyridone* was prepared when 5-phenoxy-4,6-diphenyl-2-pyrone (0·5 g.) was refluxed with hydroxylamine hydrochloride (0·5 g.) in pyridine (12 ml.) for 5 hr., and recovered by dilution with water. It crystallised from benzene in needles, m. p. 224—225°, which gave a red colour with ferric chloride but did not reduce Tollens's reagent (Found: C, 77·85; H, 4·8; N, 4·1. $C_{23}H_{17}NO_3$ requires C, 78·0; H, 4·8; N, 3·9%).

1-*Hydroxy*-4,5,6-*triphenyl*-2-*pyridone* was prepared from 4,5,6-triphenyl-2-pyrone as above and crystallised from benzene–light petroleum in plates, m. p. 232—233° (Found: C, 81·7; H, 5·1; N, 4·15. $C_{23}H_{17}NO_2$ requires C, 81·4; H, 5·05; N, 4·1%).

1-*Hydroxy*-5-*methoxy*-4-*phenyl*-6-p-*tolyl*-2-*pyridone* was prepared in 20% yield when 5-methoxy-4-phenyl-6-*p*-tolyl-2-pyrone (1 g.) was refluxed with hydroxylamine hydrochloride (1 g.) in pyridine (20 ml.) for 5 hr. The mixture was poured into water, and the product crystallised from methanol; the unchanged pyrone was recovered, leaving the pyridone in the mother liquor. The *pyridone* was recovered by dilution and crystallised from benzene–light petroleum in elongated plates, m. p. 195—196° (Found: C, 74·4; H, 5·6; N, 4·5. $C_{19}H_{17}NO_3$ requires C, 74·25; H, 5·6; N, 4·6%).

1-Hydroxy-5-methoxy-4,6-diphenyl-2-pyridone, m. p. and mixed m. p.[1] 211°, was prepared from the pyrone by the same method.

1-*Benzyloxy*-4,5,6-*triphenyl*-2-*pyridone* (IX; R = Ph).—1-Hydroxy-4,5,6-triphenyl-2-pyridone (0·7 g.) was added to a solution of sodium (0·1 g.) in ethanol (30 ml.) and refluxed with

benzyl chloride (0·5 g.) for 4 hr. The mixture was diluted with water and extracted with ether, and the ethereal solution distilled. The residual 1-benzyloxy-2-pyridone (0·4 g.) crystallised from dilute methanol in pale yellowish prismatic plates, m. p. 174—175°, which gave a negative ferric chloride test (Found: C, 83·7; H, 5·4; N, 3·25. $C_{30}H_{23}NO_2$ requires C, 83·9; H, 5·4; N, 3·3%). This 1-benzyloxypyridone (0·1 g.) was recovered unchanged after being heated with methanol (5 ml.) containing 5 drops concentrated hydrochloric acid for 30 min.

1-*Amino-5-phenoxy-4,6-diphenyl-2-pyridone* (XIVa; R = OPh).—5-Phenoxy-4,6-diphenyl-2-pyrone (0·7 g.) was refluxed with 25% hydrazine hydrate (7 ml.) for 4 hr. and, after dilution, the *aminopyridone* was recovered in 80% yield. It crystallised from dilute methanol in needles, m. p. 181° (Found: C, 77·4; H, 5·25; N, 7·8. $C_{23}H_{18}N_2O_2$ requires C, 77·9; H, 5·1; N, 7·9%). It reduces Fehling's solution and Tollens's reagent and gives a green colour with ferric chloride. This aminopyridone was also prepared in 70% yield when a solution of methyl *cis*-5-oxo-4-phenoxy-3,5-diphenylpentenoate (0·3 g.) in ethanol (15 ml.) was refluxed with 85% hydrazine hydrate (2 ml.) for 2 hr.

Action of Nitrous Acid.—A solution of the aminopyridone (0·7 g.) in glacial acetic acid (30 ml.) was treated (dropwise) with a solution of sodium nitrite (1·5 g.) in water (12 ml.). When the mixture was heated to boiling, diluted, and cooled, 5-phenoxy-4,6-diphenyl-2-pyridone, m. p. and mixed m. p. 235°, was obtained.

1-*Diacetylamino-5-phenoxy-4,6-diphenyl-2-pyridone* was prepared when the foregoing aminopyridone (0·6 g.) was heated with acetic anhydride (6 ml.) in pyridine (10 ml.) for 3 hr. It crystallised from methanol in needles, m. p. 158° (Found: C, 74·2; H, 5·2; N, 6·5. $C_{27}H_{22}N_2O_4$ requires C, 73·9; H, 5·1; N, 6·4%). When this diacetate (0·2 g.) in ethanol (20 ml.) containing hydrochloric acid (2 ml.) was refluxed for 30 min., the aminopyridone was recovered after dilution and neutralisation.

1-*Monoacetylamino-5-phenoxy-4,6-diphenyl-2-pyridone* was prepared when the foregoing diacetate (0·3 g.) was refluxed with 5% methanolic potassium hydroxide (10 ml.) for 2 hr. It separated after dilution and acidification, and crystallised from chloroform–light petroleum in needles, m. p. 234° (Found: C, 75·8; H, 4·9; N, 7·4. $C_{25}H_{20}N_2O_3$ requires C, 75·7; H, 5·1; N, 7·1%). It was soluble in aqueous sodium hydroxide, was hydrolysed to the free amine by methanolic hydrochloric acid, and did not give a colour with ferric chloride.

1-*Acetyl*-1-*methylamino-5-phenoxy-4,6-diphenyl-2-pyridone.*—A solution of 1-monoacetylamino-5-phenoxy-4,6-diphenyl-2-pyridone (0·4 g.) in 2% aqueous potassium hydroxide (100 ml.) was treated with dimethyl sulphate (4 ml.) with shaking. The desired *compound* was separated from the alkaline medium and crystallised from dilute methanol in aggregate plates, m. p. 173° (Found: C, 75·85; H, 5·2; N, 6·9; NMe, 6·8. $C_{26}H_{22}N_2O_3$ requires C, 76·1; H, 5·4; N, 6·8; NMe, 7·1%). It was recovered unchanged after 2 hr. with 3% methanolic potassium hydroxide or hydrochloric acid in boiling ethanol.

1-*Dibenzoylamino-5-phenoxy-4,6-diphenyl-2-pyridone.*—The foregoing 1-amino-2-pyridone (0·5 g.) was refluxed with benzoyl chloride (1 ml.) and anhydrous sodium carbonate (2 g.) in dry chloroform for 2 hr. The *product* recovered from the solvent was treated with cold methanol and then crystallised from benzene–light petroleum in prismatic needles, m. p. 219° (decomp.) (Found: C, 79·2; H, 4·8; N, 5·25. $C_{37}H_{26}N_2O_4$ requires C, 79·0; H, 4·7; N, 5·0%).

1-*Monobenzoylamino-5-phenoxy-4,6-diphenyl-2-pyridone.*—This *amide* was prepared by heating the dibenzoyl derivative (0·3 g.) (*a*) with methanolic potassium hydroxide as for the diacetate or (*b*) in methanol (60 ml.) containing hydrochloric acid (2 ml.) for 1 hr. It crystallised from chloroform–light petroleum in aggregate needles, m. p. 242° (Found: C, 78·5; H, 4·8; N, 5·9. $C_{30}H_{22}N_2O_3$ requires C, 78·6; H, 4·8; N, 6·1%). This derivative was also prepared by refluxing benzoyl chloride with a dry chloroform solution of the aminopyridone in presence of anhydrous potassium carbonate for 3 hr.

1-*Benzylideneamino-5-phenoxy-4,6-diphenyl-2-pyridone.*—A solution of benzaldehyde (0·5 g.) and the aminopyridone (0·4 g.) in ethanol (2 ml.) was heated on the water-bath for 2 hr. The residue was then extracted with ethanol and, after dilution with water, the *benzylidene derivative* separated. It crystallised from benzene in yellow needles, m. p. 236° (Found: C, 81·4; H, 5·1; N, 6·1. $C_{30}H_{22}N_2O_3$ requires C, 81·4; H, 5·0; N, 6·3%).

The benzylidene derivative (0·7 g.) was refluxed with 20% ethanolic potassium hydroxide (20 ml.) for 4 hr., during which ammonia was evolved. On dilution with water, 5-phenoxy-4,6-diphenyl-2-pyridone (0·45 g.) was recovered and crystallised from pyridine–methanol in needles, m. p. and mixed m. p. 233°. When the alkaline solution was extracted with chloroform,

acidified, and again extracted with chloroform, benzoic acid (m. p. and mixed m. p. 121°) was obtained. This benzylidene derivative (0·15 g.) was not hydrolysed by boiling hydrochloric acid (3 ml.) in methanol (80 ml.) for 3 hr.

1-*Furfurylideneamino-5-phenoxy-4,6-diphenyl-2-pyridone.*—This *derivative* was prepared from the aminopyridone and furfuraldehyde and crystallised from benzene–light petroleum in yellow needles, m. p. 195—196° (Found: C, 77·9; H, 4·6; N, 6·2. $C_{28}H_{20}N_2O_3$ requires C, 77·8; H, 4·7; N, 6·5%). It was hydrolysed to the pyridone and furoic acid, m. p. and mixed m. p. 131°, by boiling ethanolic potassium hydroxide.

Analogously, the 1-*amino-2-pyridones* (XIVb—f) (Table 5) were prepared from the pyrones (II) in about 70% yield and crystallised from suitable solvents. Therefrom, the diacetates,

TABLE 5.

1-Amino-2-pyridones (XIVb—f) and their derivatives.

				Found (%)				Required (%)		
	R	M. p.	Solvent †	C	H	N	Formula	C	H	N
b	*p*-Me·C_6H_4·O	202°	E	78·0	5·3	7·65	$C_{24}H_{20}N_2O_2$	78·2	5·5	7·6
b	diacetyl	164	Dil. M	73·8	5·4	6·2	$C_{28}H_{24}N_2O_4$	74·3	5·35	6·2
b	monoacetyl	258	C–L	75·75	5·4	6·8	$C_{26}H_{22}N_2O_3$	76·1	5·4	6·8
b	acetyl-methyl ...	176 [a]	Dil. M	76·2	5·65	6·5	$C_{27}H_{24}N_2O_3$	76·4	5·7	6·6
b	dibenzoyl	198 *	B–L	79·1	4·8	4·9	$C_{38}H_{28}N_2O_4$	79·2	4·9	4·9
b	monobenzoyl	150 *	B–L	78·7	5·0	5·8	$C_{31}H_{24}N_2O_3$	78·8	5·1	5·9
b	benzylidene	246 [b]	C–L	81·8	5·1	6·1	$C_{31}H_{24}N_2O_2$	81·5	5·3	6·1
b	furfurylidene	220 [b]	C–L	78·3	4·85	6·4	$C_{28}H_{22}N_2O_3$	77·8	5·0	6·3
c	*p*-Cl·C_6H_4·O	203	M	71·1	4·5	7·4	$C_{24}H_{17}ClN_2O_2$ [c]	71·05	4·4	7·2
c	diacetate	159	Dil. M	68·3	4·55	5·8	$C_{27}H_{21}ClN_2O_4$	68·55	4·5	5·9
c	furfurylidene	216 [b]	B–L	71·9	4·1	5·9	$C_{28}H_{19}ClN_2O_3$	72·0	4·1	6·0
d	*p*-Br·C_6H_4·O	222	E	63·7	3·95	6·5	$C_{24}H_{17}BrN_2O_2$ [d]	63·7	4·0	6·5
d	diacetyl	160	Dil. M	62·4	4·3	5·3	$C_{27}H_{21}BrN_2O_4$	62·65	4·1	5·4
e	C_6H_5	199	B–L	81·6	5·4	8·35	$C_{32}H_{18}N_2O$	81·6	5·4	8·3
e	diacetyl	167	Dil. M	76·5	5·1	6·7	$C_{27}H_{22}N_2O_3$	76·7	5·25	6·6
e	monoacetyl	246 [a]	Dil. M	78·7	5·15	7·4	$C_{25}H_{20}N_2O_2$	78·9	5·3	7·4
e	dibenzoyl	272 *	E	80·9	4·8	5·3	$C_{37}H_{26}N_2O_3$	81·3	4·8	5·1
e	monobenzyl	252	B–L	81·4	5·2	6·4	$C_{30}H_{22}N_2O_2$	81·4	5·0	6·3
e	benzylidene	158 [b]	M	84·3	5·3	6·65	$C_{30}H_{22}N_2O$	84·5	5·2	6·6
e	furfurylidene	183 [b]	E	80·75	4·8	6·9	$C_{24}H_{20}N_2O_2$	80·7	4·8	6·7
f	OMe [1]	186								
f	diacetyl	128	M	68·9	5·45	7·7	$C_{32}H_{26}N_2O_4$	68·6	5·4	7·45
f	benzylidene	164 [b]	B–L	79·25	5·15	7·2	$C_{28}H_{20}N_2O_2$	78·9	5·3	7·4

* With decomp. † E = ethanol; C = chloroform; other solvents as indicated before.
[a] Plates; the others formed needles. [b] Yellow. [c] Cl: Found, 9·0. Reqd., 9·1%. [d] Br: Found, 18·4. Reqd., 18·45%.

monoacetates, dibenzoates, monobenzoates, and benzylidene and furfurylidene derivatives have been prepared. Compound (XIVe) was also prepared from ethyl *trans*-β-desylcinnamate, methyl *cis*-β-desylcinnamate, or methyl β-benzoyl-αβ-diphenylacrylate, and (XIVf) from methyl *cis*-4-methoxy-5-oxo-3,5-diphenylpentenoate by the action of hydrazine hydrate.

The authors thank the Director of the Infrared Department, Sadtler's Research Laboratories, Philadelphia, for the infrared measurements of the methoxy-series, and Professors F. G. Baddar and W. I. Awad, Faculty of Science, Ein-Shams University, Cairo, U. A. R., for the other infrared determinations, also Professor Baddar for his interest in the infrared data.

CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE, ALEXANDRIA UNIVERSITY,
ALEXANDRIA, EGYPT, U.A.R. [*Received, May 2nd,* 1961.]

Vol. 1961, page 4498, Table 5, line 9 *. *For* monobenzyl *read* monobenzoyl.

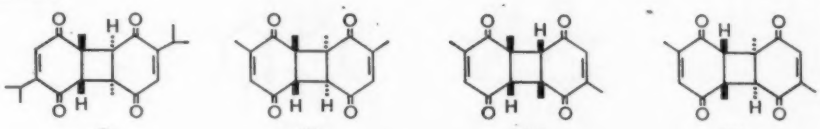
886. *Photodimers of Alkylbenzoquinones.*

By R. C. Cookson, D. A. Cox, and J. Hudec.

In sunlight the dimethylbenzoquinones dimerise by addition of the double bonds of two molecules to form a cyclobutane ring. The *trans*-dimers are stable to further irradiation, but the *cis*-dimers cyclise through a second reaction of the same sort, forming saturated, box-shaped molecules. All the dimers dissociate to the original monomers on pyrolysis.

The photodimer of thymoquinone has been known for over a century.[1] Its chemical [2] and spectroscopic [3] properties show that it is formed by the coupling of two monomer molecules to form a cyclobutane ring, and the frequency and lack of splitting of the methyl proton resonance [3] show that both methyl groups are attached to quaternary carbon atoms in the dimer: but there is no evidence on whether the monomer units are joined head-to-head or head-to-tail (as in I) or whether the two *cis*-fused cyclohexenedione rings are joined to the same side or to opposite sides of the cyclobutane ring (as in I).

Irradiation of *p*-benzoquinone or its mono-, tri-, or tetra-methyl derivative in solution or as the crystal with light from a medium-pressure mercury arc or from the sun produced no dimer: an insoluble, unsublimable polymer, containing hydroxyl groups, was slowly formed in all cases, accompanied by the corresponding quinol when the solvent had available hydrogen atoms. The three dimethylbenzoquinones, however, yielded a variety of dimers.



(I) (II) (III) (IV)

Irradiation of crystalline 2,6-dimethylbenzoquinone with sunlight gave variable results until it was realised that the main product, which was rapidly formed, was very unstable to heat: by avoiding exposure to heat during purification a yellow dimer was isolated in high yield. The dimer, which slowly dissociated back to the monomer in solution or even in the crystalline state at room temperature, showed the characteristic bis-enedione chromophore ($\lambda_{max.}$ 246 mμ, ε 22,800; $\nu_{max.}$ 1677 and 1640 cm.$^{-1}$). Its stability to further irradiation with sunlight or a mercury arc, when *cis*-dimers undergo a second cyclisation [4] (see below), suggests that this dimer has a *trans*-configuration.* The extraordinary instability to heat compared with the behaviour of compounds that can differ from it only in the position of methyl groups must be of steric origin. The unstable isomer must then be (II),† strained because of the two linked quaternary centres.

Irradiation of 2,6-dimethylbenzoquinone through Pyrex glass with a mercury arc gave none of the compound (II), but instead two other dimers; these were also produced (in higher yield) with sunlight. One, which was adsorbed rather more strongly on silica gel than the unstable dimer (II), was also yellow, the other was colourless, sparingly soluble, and very high-melting. Structure (VII) will be established for the colourless dimer when it is considered below, with the dimers of the same kind from the other two dimethylbenzoquinones. The second yellow dimer also showed the bis-enedione chromophore

* In the rest of this paper we use *cis* to denote dimers with both enedione groups on the same side of the cyclobutane ring, and *trans* for those with the enedione groups on opposite sides, assuming that individual ring-fusions are invariably *cis*.

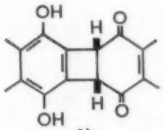
† All the compounds described here are racemic, formulæ showing only one form.

[1] Lallemand, *Ann. Chim. Phys.*, 1857, **49**, 167.
[2] Smith and Tess, *J. Amer. Chem. Soc.*, 1944, **66**, 1323, who give earlier references.
[3] Zavarin, *J. Org. Chem.*, 1958, **23**, 47.
[4] See also Cookson, Crundwell, and Hudec, *Chem. and Ind.*, 1958, 1003.

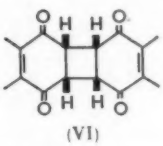
($\lambda_{max.}$ 237 mμ, ε 15,000; $\nu_{max.}$ 1685, 1662, and 1630 cm.$^{-1}$), but in sharp contrast with the unstable dimer (II) it did not decompose at 200°. Further irradiation of this dimer induced fast and quantitative cyclisation to the saturated dimer (VII). Since 2,6-dimethylbenzoquinone itself under the same conditions gave the saturated dimer (VII) more slowly and in much lower yield, the change cannot involve dissociation and recombination. The dimer, therefore, has the *cis*-configuration. Its being merely the *cis*-isomer of the unstable dimer (II) would hardly explain the far slower dissociation. It must then be the alternative *cis*-dimer (III), free from the source of strain present in (II).

Sunlight converted crystalline 2,5-dimethylbenzoquinone in fairly good yield into a mixture of two dimers, one yellow, the other colourless. Under a mercury lamp the colourless isomer only was formed, and in poor yield. On the other hand, ultraviolet irradiation of a solution of the quinone in ethyl acetate gave some of the yellow isomer. Above its m. p. (164°) this yellow dimer dissociated to the monomer. Its stability to further irradiation in the crystal or in solution suggests that it has the *trans*-configuration, and its thermal stability compared with that of dimer (II) showed that the methyl groups on the cyclobutane ring are 1,3-, not 1,2-. It therefore probably has the structure (IV).[5]

Fieser and Ardao,[6] during their work on the quinone antibiotic from the arachnid Gonyleptide, noticed incidentally that sunlight bleached 2,3-dimethylbenzoquinone to a white, insoluble polymer. We found that exposure of the crystalline quinone to sunlight soon gave a mixture of a yellow and a colourless dimer, the proportion of the latter increasing with the time of exposure. The same products were formed more slowly, less



(V)



(VI)

cleanly, and in lower yield when a mercury arc was used. Further exposure of the yellow dimer ($\lambda_{max.}$ 248 mμ, ε 17,600; $\nu_{max.}$ 1677 and 1607 cm.$^{-1}$) to light from the sun or the arc gave a quantitative yield of the colourless one [shown below to have structure (IX)]. Since the colourless dimer was formed more rapidly and smoothly from the yellow dimer than from the monomer, the yellow dimer must have the *cis*-configuration. That it had at least two hydrogen atoms on the cyclobutane ring followed from its enolisation to the quinol (V), which gave a diacetate. Comparison of the infrared spectrum of the dimer in the range 1200—1500 cm.$^{-1}$ with spectra of model compounds indicated that it was too simple to come from a molecule containing tertiary methyl groups: in fact the spectrum was very similar to that of monomeric 2,3-dimethylbenzoquinone (see Table). The resulting structure (VI) was clinched by the proton magnetic resonance spectrum (kindly measured by Dr. L. Pratt) which had two sharp peaks at $\tau = 6{\cdot}10$ and $8{\cdot}12$ in the ratio 1 : 3. We are now trying to convert the quinol (V) and the dimer (VI) into derivatives of cyclobutadiene.

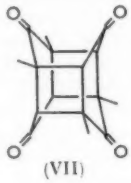
Since the dimer of thymoquinone is relatively stable to heat and does not yield a saturated isomer on further irradiation it probably has the *trans*-structure with 1,3-methyl groups (I).

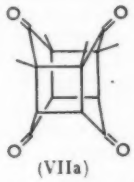
The structures of the three colourless dimers still have to be considered. All were high-melting (or decomposing), sparingly soluble solids that sublimed *in vacuo*, and were clearly all of the same structural type. Their general structure follows from these facts: (1) They are saturated to the usual chemical tests, and show only low end-absorption in the ultraviolet region. (2) They each have a strong band in the infrared spectrum between 1700 and 1715 cm.$^{-1}$. (3) The *cis*-dimers (III) and (VI) form the respective colourless

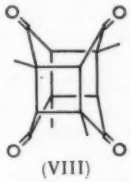
[5] Cookson and Hudec, *Proc. Chem. Soc.*, 1959, 11.
[6] Fieser and Ardao, *J. Amer. Chem. Soc.*, 1956, **78**, 774.

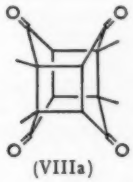
dimers on irradiation, and appear to be intermediates in their formation from the quinones. (4) Each dissociates to its own monomer on pyrolysis. (5) Although the sublimed dimers are anhydrous and contain no hydroxyl groups, they crystallise from solvents such as ethyl acetate as dihydrates which betray by their infrared spectra the presence of hydrogen-bonded hydroxyl groups (3270 $cm.^{-1}$), C–O bonds (1035 $cm.^{-1}$), and lower-frequency carbonyl groups (1690—1700 $cm.^{-1}$). These properties can be explained only by their formation from two molecules of quinone combining at both double bonds, without rearrangement.

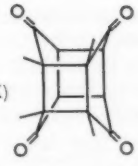
Each dimethylquinone could give two such saturated dimers. If the one from 2,6-dimethylquinone is really formed from compound (III) it must have structure (VII). Pyrolysis of the dimer in the gas phase at 450° gave pure 2,6-dimethylquinone; the infrared spectrum of the total product was identical with that of an authentic sample. Gas chromatography also showed only 2,6-dimethylquinone, although synthetic mixtures of 2,6-dimethylquinone containing small proportions of benzoquinone and duroquinone were well separated. However, this cannot be taken as additional evidence in favour of structure (VII) rather than the alternative (VIIa) because the latter might well cleave almost entirely in the vertical plane, rather than horizontally, because of repulsion between the methyl groups * (cf. the much greater speed of cleavage of II than of III, IV, or VI).


(VII)


(VIIa)


(VIII)


(VIIIa)

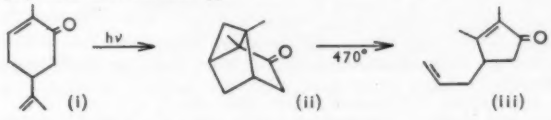

(IX)

(X)

Pyrolysis of the colourless dimer from 2,5-dimethylquinone also gave entirely the parent quinone, with no detectable trace of 2,3-dimethylquinone, but again a compound (VIIIa) might split preferentially in the horizontal plane, so that the evidence is not decisive in favour of (VIII). Since no intermediate *cis*-dimer could be isolated in this case, the structure of the colourless dimer must be left in doubt. (In fact it could be argued that the failure to isolate the " half-shut " *cis*-dimer tends to favour VIIIa.)

Pyrolysis of the colourless isomer from 2,3-dimethylquinone gave only the parent quinone, free from any detectable trace of 2,5-isomer. Again, this in itself does not quite exclude (VIIIa), but the synthesis of the dimer from compound (VI) is sufficient proof of structure (IX).

* This expectation is justified only by the symmetry of the ring system in (VIIa): it does not imply that cyclobutanes in bridged-ring structures will always split between quaternary centres. If it releases greater angle-strain, the alternative cleavage may take place—for example,[7] carvonecamphor (ii) gives the cyclopentenone (iii) instead of carvone (i).



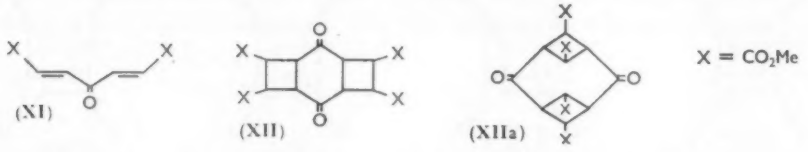
(i) (ii) (iii)

Büchi and Goldman, *J. Amer. Chem. Soc.*, 1957, **79**, 4741.

Very recently there appeared a contradictory account [8] of the photodimerisation of 2,3-dimethylbenzoquinone. It was reported, as we have found, to be converted by sunlight into a yellow dimer that on further irradiation gave a colourless one. Except that the carbonyl band of the yellow dimer is rather higher in frequency than that of ours, the properties of the two pairs of isomers make it possible that they are the same. Yet the colourless dimer was said to give 2,5-dimethylbenzoquinone on pyrolysis, requiring structure (VIIIa). If the product of pyrolysis was correctly identified, there seem to be only two likely explanations for the discrepancy: (1) we have used different crystal forms of 2,3-dimethylbenzoquinone, leading to different dimers, or (2) the pyrolysis was carried out under conditions that rearrange 2,3-dimethylbenzoquinone to the 2,5-isomer. We could detect no 2,5-dimethylbenzoquinone when the 2,3-isomer or its dimer was heated in the gas phase or in a sealed tube at temperatures from 300° to 700°.

The photo-dimer of 2,6-dimethyl-4-pyrone has recently been shown [9] to have an analogous structure (X).

Dimethyl 4-oxohepta-2,5-dienedioate (XI) is converted by sunlight into a saturated dimer [10] for which Stobbe and Färber suggested the structure (XII). They did not consider the alternative (XIIA), which could also arise by formation of two cyclobutane rings. In an attempt to distinguish between the two possibilities, either of which would be consistent with the ultraviolet and infrared spectra, we pyrolysed the dimer.* Dimethyl fumarate



(XI) (XII) (XIIa)

was easily isolated but, although the pyrolysate had the characteristic pungent smell, benzoquinone could not be identified and the infrared spectrum of the total product showed that it could not have been present in more than traces. Nevertheless the formation of dimethyl fumarate decides in favour of Stobbe and Färber's structure (XII), and the proton magnetic resonance spectrum is reported to be consistent with this structure.[11] Irradiation of a solution of benzoquinone in dimethyl fumarate gave a product with an infrared spectrum very similar to that of the dimer (XII). Incidentally it was noticed that irradiation of dimethyl fumarate led to tetramethyl *cis-trans-cis*-cyclobutanetetracarboxylate in good yield, as mentioned later by Griffin, Basinski, and Vellturo.[12] All attempts to

Infrared maxima (cm.$^{-1}$) for mulls in tetrachloroethylene.

BQ = 1,4-Benzoquinone. A = 2-Methyl-3-phenylcholest-2-ene. B = 3-Methylcholest-2-ene.

2,3-Me_2 BQ	(VI)	2,6-Me_2 BQ	(III)	2,5-Me_2 BQ	(IV)	Thymoquinone	(I)	A	B
1243	1290	1292	1290	1300	1330 *	1310	1295	1302	1323 *
1305	1305	1317	1320 *	1355	1350	1358	1335	1330	1330
1358	1335	1363	1350	1383	1368	1385 *	1360	1345	1345
1375	1370	1383	1378	1438 *	1380	1390	1370	1364 *	1365 *
1435	1435	1435 *	1405	1447	1385 *	1435	1380	1377	1380
		1442	1432		1433	1450	1445	1440	1445
			1456			1470	1458	1465	1465

* Shoulder.

* We are indebted to Dr. R. G. Lingard for these experiments.

[8] Flaig, Salfeld, and Llanos, *Angew. Chem.*, 1960, **72**, 110.

[9] Yates and Jorgensen, *J. Amer. Chem. Soc.*, 1958, **80**, 6150.

[10] Straus, *Ber.*, 1904, **37**, 3293; Stobbe and Färber, *Ber.*, 1925, **58**, 1548; Midorikawa, *Bull. Chem. Soc. Japan*, 1953, **26**, 302.

[11] Corse, Finkle, and Lundin, *Tetrahedron Letters*, 1961, No. 1, 1.

[12] Griffin, Basinski, and Vellturo, *Tetrahedron Letters*, 1960, No. 3, 13; see also Criegee and Höver, *Chem. Ber.*, 1960, **93**, 2521.

convert the central ring of the dimer (XII) into the quinone or a derivative of the quinone failed.

Experimental

Ultraviolet spectra of ethanol solutions were recorded on a Unicam S.P. 700 and infrared spectra of Nujol mulls on a Unicam S.P. 100 spectrophotometer.

The compounds were irradiated at room temperature through Pyrex glass with a 125-w medium-pressure mercury arc or with sunlight. A thin deposit of crystals for irradiation was obtained by evaporating a solution of the sample in ether on the inside of a relatively large flask.

The various quinones were prepared by standard methods. Toluquinone was prepared from its quinol by oxidation with sodium dichromate in dilute sulphuric acid. Duroquinone was obtained from durene through the dinitro- and diamino-intermediates, according to Smith's method.[13] Trimethylbenzoquinone and the three dimethylbenzoquinones were prepared by oxidation of the corresponding phenols with Fremy's salt.[14]

Toluquinone.—The quinone gradually became brown on irradiation by a mercury lamp or by the sun. After 3 days the product was shaken with a small quantity of ether, and the insoluble brown solid was filtered off. The quinone obtained on evaporation of the filtrate was again irradiated. The solid, accumulated from several such cycles, did not crystallise, but was precipitated from ether by addition of light petroleum (b. p. 40—60°). It began to decompose at about 300°. It did not sublime under a vacuum. The ill-defined infrared spectrum showed peaks due to hydroxyl groups at 1200 and 3400 cm.$^{-1}$, and a max. at 1655 with shoulders at 1740 and 1620 cm.$^{-1}$.

Duroquinone.—The similar, pale brown product from duroquinone was insoluble in all the usual organic solvents. It began to decompose at about 300°, without producing duroquinone. The rather diffuse infrared spectrum again showed the presence of hydroxyl groups: $\nu_{max.}$ 3350, 1725, 1680, 1645sh cm.$^{-1}$.

Trimethyl-1,4-benzoquinone.—Melting of the quinone (32°) was prevented by a finger cooled with ice and salt inserted into the dry nitrogen-filled flask on the inside of which the crystals of quinone had been deposited. After 1½ days' exposure during intermittent sunlight the product was dissolved in ether. Addition of a small amount of light petroleum (b. p. 40—60°) precipitated a white substance: the unchanged quinone was then recycled. The product, which could not be sublimed, melted with decomposition at about 160° and had $\nu_{max.}$ 3400, 1700, and 1620sh cm.$^{-1}$.

Irradiation of 2,5-Dimethylbenzoquinone.—After 4—8 hours' exposure to sunlight the colour of the crystalline quinone had faded considerably. The product was digested with boiling ether and the white substance (A) filtered off. The residue obtained on evaporation of the filtrate was chromatographed in benzene on silica gel. Unchanged quinone, m. p. 125°, was eluted with benzene. Benzene containing 10% of ethyl acetate eluted the *trans*-dimer (IV), 1α,2β,7β,8α-1,4,7,10-*tetramethyltricyclo*[6,4,0,0^{2,7}]*dodeca*-4,10-*diene*-3,6,9,12-*tetraone* [1,4,4a,4bβ,5,8,8a,8bβ-*octahydro*-2,4aα,6,8aβ-*tetramethyl*-1,4,5,8-*tetraoxobiphenylene*], which crystallised from ether in pale yellow needles, m. p. 163—164° (Found: C, 70·8; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%), $\lambda_{max.}$ 240 mμ (ε 21,750) $\nu_{max.}$ 1680, 1645, and 1620 cm.$^{-1}$. At the m. p. a yellow sublimate of monomeric quinone condensed on the cooler part of the tube. The infrared spectrum of a sample of the dimer (IV) that had been irradiated with a mercury arc for 12 hr. was unchanged.

The white substance (A) was extracted with light petroleum (b. p. 40—60°) in a Soxhlet apparatus for several days; a pale yellow extract was obtained, which yielded more dimer (IV). The white, insoluble solid, purified by vacuum-sublimation, had an infrared spectrum identical with that of the box-dimer (VIII) made by irradiation with a mercury arc, the yield in the latter process being much smaller.

The yields of dimers (IV) and (VIII) obtained by sunlight irradiation varied according to the length of exposure and the amount of sunlight. Optimum yields were: *trans*-dimer (IV) *ca.* 40%; box-dimer (VIII) *ca.* 2%; recovered quinone *ca.* 40%.

The white solid, insoluble in ether, collected from many irradiations of the quinone with a

[13] Smith, *Org. Synth.*, **10**, 40.
[14] Teuber and Rau, *Chem. Ber.*, 1953, **86**, 1036.

mercury arc, was extracted (Soxhlet) with ethyl acetate for 6 days. Colourless needles of the box-dimer (VIII), 1,4,7,10-*tetramethylpentacyclo*[6,4,0,$0^{2,7}$,$0^{4,11}$,$0^{5,10}$]*dodeca*-3,6,9,12-*tetraone*, separated from the concentrated solution. They decomposed at about 250°, when the yellow monomer sublimed up the tube leaving a dark residue. At 240°/20 mm. the compound sublimed to a white powder (Found: C, 70·8; H, 6·0%); it had $\nu_{max.}$ 1700 cm.$^{-1}$ (with shoulder at 1715 cm.$^{-1}$).

This, and the other two box-dimers described below, rapidly absorbed moisture from the air, even in the crystalline state. Samples then absorbed strongly in the regions of 3300 and 1040 cm.$^{-1}$ and the frequency of the C=O vibration fell. Correct analyses were obtained only when freshly sublimed samples were sealed and preserved packed in silica gel. A 12 month-old sample of box-dimer (VIII) had an infrared spectrum with $\nu_{max.}$ 1690, 1030, and 3300 cm.$^{-1}$. A sample recrystallised from ethyl acetate and dried in air gave analyses for a *dihydrate* (Found: C, 62·7; H, 6·5. $C_{16}H_{16}O_4,2H_2O$ requires C, 62·3; H, 6·5%).

Pyrolysis.—The dimer (VIII) was slowly vaporised at 235° in a stream of nitrogen (4 cm. Hg pressure) that passed through a furnace at 500° and then through a cold trap. The unfractionated product had an infrared spectrum identical with that of 2,5-dimethylbenzoquinone. A mixture of 5% of 2,3-dimethylbenzoquinone in the 2,5-dimethylquinone clearly showed a peak at 830 cm.$^{-1}$ due to the 2,3-isomer.

Irradiation of 2,3-*Dimethylbenzoquinone.*—The crystalline quinone was exposed to sunlight and then extracted with boiling ether. The cream-coloured solid (B) was removed and the filtrate evaporated. On chromatography of the residue on silica gel, unchanged quinone passed through in benzene. Benzene containing 10% of ethyl acetate eluted the *cis*-dimer (VI), 1α,2α,7α,8α-4,5,10,11-*tetramethyltricyclo*[6,4,0,$0^{2,7}$]*dodeca*4,10-*dien e*-3,6,9,12-*tetraone*, which crystallised from ether in pale yellow cubes, m. p. 163—164° (without decomposition or sublimation) (Found: C, 70·5; H, 5·85%), $\lambda_{max.}$ 248 mμ (ε 17,570), $\nu_{max.}$ 1677 and 1607 cm.$^{-1}$ (cf. Table).

The extract from several days' Soxhlet-extraction of the solid (B) yielded more of the dimer (VI). The insoluble white residue of the box-dimer (IX), 1,2,7,8-*tetramethylpentacyclo*-[6,4,0,$0^{2,7}$,$0^{4,11}0^{5,10}$]*dodeca*-3,6,9,12-*tetraone*, was purified by sublimation at 240°/20 mm. (Found: C, 70·25; H, 5·8%). It began to decompose at *ca.* 270° with formation of a trace of yellow sublimate. The sublimed dimer had $\nu_{max.}$ 1710 cm.$^{-1}$; the colourless needles that crystallised from ethyl acetate had $\nu_{max.}$ 1700, 1035, and 3270 cm.$^{-1}$.

Further irradiation of the *cis*-dimer (VI) with a mercury lamp gave a quantitative yield of the box-dimer (IX).

In a typical experiment, 2,3-dimethylbenzoquinone (5·5 g.) was exposed to winter sunshine for about 2 hr., and the yields obtained were: recovered quinone (2·3 g.) 42%; *cis*-dimer (VI) (1·4 g.) 26%; box-dimer (IX) (0·11 g.) 2%. Longer illumination increased the yield of box-dimer (IX) at the expense of (VI). Light from a mercury arc gave a much lower yield of (VI) (about 10%), and a greater yield of (IX) (about 5%) for a 24 hr. irradiation.

Pyrolysis.—The box-dimer (IX) at 240° was vaporised in a slow stream of nitrogen at 8 cm. passing through a tube heated at 510°. The total product collected in the cold trap had a spectrum superimposable on that of 2,3-dimethylbenzoquinone. A synthetic mixture of 5% of 2,5-dimethylbenzoquinone in the 2,3-isomer had a spectrum that clearly showed peaks due to the former at 1350, 1250, 1005, and 920 cm.$^{-1}$.

Irradiation of 2,6-*Dimethylbenzoquinone.*—After 1—2 hours' exposure to sunlight the quinone had faded to a pale yellow colour and the product was quickly extracted with cold ether. The pale yellow solid that was filtered off was immediately crystallised from ether. The pale yellow crystals of 1α,2β,7β,8α-1,2,4,11-*tetramethyltricyclo*[6,4,0,$0^{2,7}$]*dodeca*-4,10-*diene*-3,6,9,12-*tetraone* (II) (70% yield) had m. p. 84°, $\nu_{max.}$ 1677 and 1640 cm.$^{-1}$. Above the m. p. the dimer dissociated to the monomer, which sublimed up the tube in yellow crystals, m. p. 71—72°. A mixture of monomer and dimer melted at 69—71°, the slightness of the depression being presumably due to rapid dissociation to the monomer in the melt. In boiling benzene the dimer soon dissociated. The ultraviolet spectrum of a dilute solution of the dimer in ethanol measured at intervals showed slow dissociation to the monomer at room temperature; time, $\lambda_{max.}$, and "ε" (calculated as dimer) were: 25 min., 246 mμ, 22,800; 50 min., 247 mμ, 22,800; 4 hr. 25 min., 252 mμ, 25,900; 24 hr., 254 mμ, 32,100; 84 hr., 255 mμ, 34,500. The quinone has $\lambda_{max.}$ 255 mμ, ε 18,300.

When the illuminated quinone was extracted with boiling ether a small amount (about

0·5% yield) of the insoluble box-dimer (VII), 1,5,7,11-*tetramethylpentacyclo*[6,4,0,$0^{2,7}$,$0^{4,11}$,$0^{5,10}$]-*dodeca*-3,6,9,12-*tetraone*, remained. It was purified by sublimation at 225—235°/20 mm., then having $\nu_{max.}$ 1700, 1715(sh) cm.$^{-1}$ (Found: C, 70·7; H, 5·9%). At atmospheric pressure the dimer (VII) sublimed unchanged at 240—300°. At 300° it began to decompose, forming only a trace of volatile yellow product.

Pyrolysis.—The vapour of the dimer (VII), preheated to 200°, was passed in a stream of nitrogen through a furnace at 450°. The yellow needles of quinone in the cold trap were dissolved in ether. Analysis by gas chromatography on silicone at 150° showed only one sharp peak, corresponding to 2,6-dimethylbenzoquinone. A mixture of 2,6-dimethyl- 70%, tetramethyl- 15%, and unsubstituted benzoquinone 15% gave three well-separated peaks in the correct ratio.

Chromatography of the ether extract from sunlight-irradiated quinone on silica gel in ether yielded the unstable dimer (II) and regenerated quinone, followed by the *cis*-dimer (III), 1α,2α,7α,8α-1,5,7,11-*tetramethyltricyclo*[6,4,0,$0^{2,7}$]*dodeca*-4,10-*diene*-3,6,9,12-*tetraone* (5% yield). It separated from ether in pale yellow cubes, m. p. 166—168°, $\lambda_{max.}$ 238 mμ (ε 15,000), $\nu_{max.}$ 1685, 1662, and 1630 cm.$^{-1}$ (Found: C, 71·0; H, 6·1%). It did not decompose or sublime at 200° at atmospheric pressure.

Irradiation of 2,6-dimethylbenzoquinone with a mercury arc for 36 hr. gave small yields of the dimers (III) and (VII). Chromatography on a silica gel column of the residue obtained on evaporation of the ether extract gave with benzene as eluent a 76% yield of recovered quinone. With 10% of ethyl acetate in benzene, the *cis*-dimer (III) was obtained (0·5%). Irradiation of the *cis*-dimer (III) with the arc for 1 hr. caused considerable bleaching, and continued irradiation led to quantitative conversion into the colourless box-dimer (VII) (identical infrared spectra). Similar irradiation of crystals of the unstable dimer (II) turned it green after about ½ hr., although its infrared spectrum was unchanged. On further irradiation the colour gradually changed to yellowish-brown: the same peaks persisted in the spectrum but became more and more diffuse.

Enolisation of the cis-*Dimer* (VI).—The *cis*-dimer (VI) (0·76 g.) was dissolved in ethanol (60 ml.), and a few drops of 2·0N-aqueous sodium hydroxide were added with shaking. The colour of the solution immediately changed from pale yellow to dark brown. After 2 hr., the solution was acidified with a few drops of dilute sulphuric acid, becoming deep yellow. It was then diluted with water and extracted with ether, the ether extract being washed in turn with sodium hydrogen carbonate solution and water. It was then dried (Na_2SO_4) and evaporated to a brown gum, which was chromatographed in benzene on silica gel. Elution with benzene containing 5% of ethyl acetate gave 3,6-*dihydroxy*-1α,8α-4,5,10,11-*tetramethyltricyclo*[6,4,0,$0^{2,7}$]*dodeca*-2,4,6,9-*tetraene*-9,12-*dione* (V) that crystallised as orange-red needles (0·19 g.), m. p. 225—226°, from methanol. The red needles were converted into a yellow, powdery form on drying *in vacuo* (Found: C, 70·4; H, 5·9%); they had λ 219 (ε 15,800sh), $\lambda_{max.}$ 256 (ε 12,100), λ 284 (ε 2500sh), $\lambda_{max.}$ 403 mμ (ε 616), $\nu_{max.}$ 1662, 1618, 1088, and 3330 cm.$^{-1}$.

Compound (V) (50 mg.) was dissolved in a 4 : 1 mixture (5·0 ml.) of pyridine–acetic anhydride. After a few minutes the orange colour began to fade, and soon the solution was almost colourless. About 12 hr. later the mixture was poured into water and extracted with ether, the ether extract being washed in turn with dilute sulphuric acid, aqueous sodium hydrogen carbonate, and water. It was then dried (Na_2SO_4) and evaporated to a white solid, which was chromatographed in benzene on silica. Elution with 5% of ethyl acetate in benzene gave the *diacetate* as very pale yellow crystals [from light petroleum (b. p. 40—60°)] (32 mg.), m. p. 165—166° (Found: C, 67·7; H, 5·5. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·7%), $\lambda_{max.}$ 255 (ε 12,400), 368 mμ (ε 207), $\nu_{max.}$ 1762, 1675, and 1615 cm.$^{-1}$.

Tetramethyl 2,7-Dioxotricyclo[6,2,0,$0^{3,6}$]decane-4,5,9,10-tetracarboxylate [10] (XII) [m. p. 239° (decomp.); $\nu_{max.}$ 1757, 1739, and 1717 cm.$^{-1}$; no intense ultraviolet absorption above 210 mμ] was vaporised in a stream of nitrogen and passed through a silica tube heated at 650°. A pale yellow solid was deposited on the cooler parts of the exit tube. Colourless crystals separated by fractional sublimation down the tube had m. p. 101—102°, unchanged when mixed with dimethyl fumarate. Their infrared spectra were also identical. The condensate from the bend in the exit tube and from the cold (liquid oxygen) trap had a pungent smell like that of benzoquinone, although its presence could not be confirmed by infrared spectra. In a control experiment a 1 : 1 mixture of dimethyl fumarate and benzoquinone passed through the furnace almost unchanged.

We acknowledge with gratitude an I.C.I. Research Fellowship (J. H.) and a D.S.I.R. Studentship (D. A. C.), and also the loan of a spectrometer from the Royal Society. The investigation was supported in part by the U.S. Air Force (Geophysics Research Directorate, A.R.D.C.) through its European Office.

THE UNIVERSITY, SOUTHAMPTON. [*Received, May 9th,* 1961.]

---

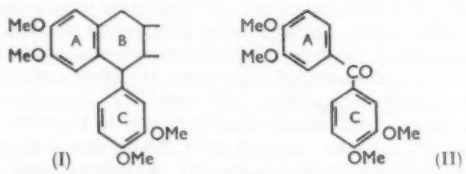
887. *Lignans. Part I. Acylation in Polyphosphoric Acid as a Route to Intermediates.*

By D. C. AYRES and R. C. DENNEY.

Phenols and their ethers with alkyloxybenzoic acids in polyphosphoric acid yield esters or benzophenones; the latter are intermediates in prospective syntheses of phenyltetrahydronaphthalene lignans.

Phosphorylation was found to affect the course of some reactions.

PODOPHYLLOTOXIN and some other lignans of its class have attracted attention because of their activity as cancer inhibitors;[1] their chemistry has been reviewed by Hartwell and Schrecker.[2] The lignan iso-olivil is inactive in therapy, but is readily available[3] in high yield from olivil of the resin of *Olea europa* and may prove a useful precursor for synthesis of active analogues. Iso-olivil dimethyl ether (I) undergoes oxidative degradation to 3,3′,4,4′-tetramethoxybenzophenone (II), and lignan synthesis by elaboration of suitably substituted alkyloxybenzophenones of this type (II) has been explored[4] and successfully concluded by Gensler *et al.* in their synthesis of picropodophyllin.[5]



Details of ring B substituents are omitted.

We find that phenolic ethers and alkyloxybenzoic acids in polyphosphoric acid give benzophenones, whereas phenols are esterified under similar conditions: Nakazawa and Kusuda[6] noted that phenol itself is esterified, not acylated, in its reaction with benzoic acid.

Synthesis of benzophenones, as lignan precursors, is better effected in polyphosphoric acid than by the normal Friedel–Crafts reaction. For instance, Traverso has described a four-step synthesis of 4-hydroxy-3,3′,4′-trimethoxybenzophenone, m. p. 50—60° (an intermediate in the synthesis of iso-olivil methyl ether), and we find that direct reaction between veratrole and vanillic acid in polyphosphoric acid is preferable, giving the ketone with m. p. 142—143°, in good yield: methylation of an alkaline solution of this compound precipitated 3,3′,4,4′-tetramethoxybenzophenone,[7] m. p. 144°, as reported by Traverso.[8]

[1] Kelly and Hartwell, *J. Nat. Cancer Inst.*, 1954, **14**, 967.
[2] Hartwell and Schrecker, "Progress in the Chemistry of Organic Natural Products," Springer, Vienna, 1958, Vol. XV, p. 83.
[3] Koerner and Carnelutti, *Rend. R. Inst. Lomb. Sci.*, 1882, **15**, II, 654.
[4] Walker, *J. Amer. Chem. Soc.*, 1953, **75**, 3390.
[5] Gensler, Samour, Wang, and Johnson, *J. Amer. Chem. Soc.*, 1960, **82**, 1714.
[6] Nakazawa and Kusuda, *J. Pharm. Soc. Japan*, 1955, **75**, 257.
[7] Kostanecki and Tambor, *Ber.*, 1906, **39**, 4026; Perkin and Weizmann, *J.*, 1906, **89**, 1661.
[8] Traverso, *Gazzetta*, 1957, **87**, 67.

XUM

Acylation of veratrole by trimethylgallic acid under similar conditions furnished 3,3',4,4',5-pentamethoxybenzophenone [7] (95% yield); this ketone is related to sikkimotoxin [9] and has been derived from the partly characterised lignan acid, plicatic acid.[10]

A monofunctional ether, anisole, was readily acylated by vanillic acid to give 4-hydroxy-3,4'-dimethoxybenzophenone, obtained earlier in an impure condition by Traverso;[8] methylation to the known 3,4,4'-trimethoxybenzophenone [7] confirmed the orientation of the product. Reaction between the trimethyl ethers of pyrogallol and gallic acid afforded 2,3,3',4,4',5'-hexamethoxybenzophenone, a degradation product of lyoniresinol dimethyl ether.[11]

A difficulty in synthesis of methylenedioxybenzophenones, precursors of the podophyllotoxin group, has been the ready fission of the ether residue by the action of Lewis acids,[12] but a satisfactory acylation of methylenedioxybenzene was described recently.[5] We tried to achieve this result by acylation in polyphosphoric acid, but failed because of rapid cleavage of the ether. The diphenylmethylene group has been used [13] to protect phenolic hydroxyl groups in the partial esterification of gallic acid, but was not retained under the conditions we used in an attempted acylation of diphenylmethylenedioxybenzene, since an ester, identical with that formed from catechol, was obtained. Catechol formed monoesters in its reaction with syringic and trimethylgallic acid, and the monoester of the latter was also the product when boron trifluoride was tested as an acylation catalyst. The free hydroxyl group of the trimethylgallic ester was readily methylated, but it could not be further esterified in polyphosphoric acid by treatment with a second equivalent of trimethylgallic acid. The diester [14] was, however, prepared by fusion of catechol and trimethylgalloyl chloride; its behaviour in the Fries reaction was similar to that reported [15] for catechol dipropionate, since catechol and syringic acid were isolated.

Phosphorylation of free hydroxyl groups is known [16] to occur in polyphosphoric acid, and quinol phosphate has been made recently [17] in this way. In two instances we found that phosphorylation affected the course of reaction: pyrogallol trimethyl ether and gallic acid yielded 3',4',5'-trihydroxy-2,3,4-trimethoxybenzophenone, but the product was only extractable from the aqueous liquors after they had been acidified with hydrochloric acid and refluxed, behaviour which is consistent with phosphorylation of free phenolic hydroxyl groups before or after acylation. Further, a phosphorus-containing polymer was the product from guaiacol and vanillic acid; their recovery on alkaline hydrolysis indicated that they had become associated through phosphate ester linkages. It is possible that the hydroxyl group of catechol half-esters is blocked by phosphorylation; if so, hydrolysis of the phosphate must occur in the acid liquor obtained during working up; the acid-catalysed hydrolysis of salol phosphate [18] provides a formal analogy with this postulated behaviour.

Experimental

Infrared absorption spectra were measured for Nujol mulls.

Polyphosphoric acid was prepared by mixing phosphorus pentoxide (8 parts by weight) with 90% orthophosphoric acid (*d* 1·75; 5 parts by volume) and was stirred at 85° for 30 min. before use.

4-Hydroxy-3,3',4'-trimethoxybenzophenone.—A mixture of vanillic acid (5·0 g., 0·03 mole) and veratrole (4·1 g., 0·034 mole) was stirred into polyphosphoric acid (from 50 g. of phosphorus

[9] Chatterjee and Chakravarti, *J. Amer. Pharmaceut. Assoc.* (*Sci. Edn.*), 1952, **41**, 415.
[10] Gardner, MacDonald, and MacLean, *Canad. J. Chem.*, 1960, **38**, 2387.
[11] Yasue and Kato, *Chem. and Pharm. Bull. Japan*, 1960, **9**, 844.
[12] Gensler and Stouffer, *J. Org. Chem.*, 1958, **23**, 909 and refs. cited.
[13] Haworth, Pedler Lecture, Jan. 1961, *Proc. Chem. Soc.*, in the press.
[14] Pepe, *Anales Asoc. quím. argentina*, 1940, **28**, 34.
[15] Awad, El-Neweihy, and Selim, *J. Org. Chem.*, 1958, **23**, 1783.
[16] Cherbuliez, Probst, and Rabinowitz, *Helv. Chim. Acta*, 1960, **43**, 464, and earlier papers in the series.
[17] Wieland and Patterson, *Chem. Ber.*, 1959, **92**, 2917.
[18] Chanley, *J. Amer. Chem. Soc.*, 1952, **74**, 4347.

pentoxide); the solution was kept at 80—83° for 30 min. and then poured into ice-water (250 ml.); the *ketone* (8·0 g., 96%) separated as a pink solid. After three recrystallisations from aqueous alcohol (1 : 1) white needles, m. p. 142—143°, were obtained (Found: C, 66·9; H, 5·6. $C_{16}H_{16}O_5$ requires C, 66·8; H, 5·6%), having $\nu_{max.}$ 3300 (broad band, bonded OH) and 1669 cm.$^{-1}$ (C=O).

The ketone (1·0 g.) in 3% aqueous sodium hydroxide was shaken with dimethyl sulphate (1·0 g.) at room temperature for 15 min. The precipitated 3,3′,4,4′-tetramethoxybenzophenone [7] (0·81 g., 77%) formed rhombs, m. p. 144°, from ethanol (Found: C, 67·4; H, 5·9. Calc. for $C_{17}H_{18}O_5$: C, 67·5; H, 6·0%), $\nu_{max.}$ 1635 cm.$^{-1}$ (C=O).

3,3′,4,4′,5-Pentamethoxybenzophenone.—Trimethylgallic acid (4·6 g., 0·023 mole) and veratrole (3·0 g., 0·025 mole) were treated in polyphosphoric acid (from 35 g. of phosphorus pentoxide) as described above. The product [7] (6·9 g., 95%) crystallised from ethanol as needles, m. p. 118—119° (Found: C, 65·1; H, 6·1. Calc. for $C_{18}H_{20}O_6$: C, 65·1; H, 6·1%), $\nu_{max.}$ 1630 cm.$^{-1}$ (C=O).

4-Hydroxy-3,4′-dimethoxybenzophenone.—This *ketone* was obtained as a syrup (8 g., 84%) which rapidly solidified, when vanillic acid (5 g.) and anisole (3·2 g.) were treated in polyphosphoric acid (from 50 g. of phosphorus pentoxide) as before. Recrystallisation from ethanol furnished needles, m. p. 109—110° (Found: C, 69·8; H, 5·5. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%), $\nu_{max.}$ 3300b and 1635 cm.$^{-1}$.

The ketone (1·0 g.) was methylated with dimethyl sulphate (0·8 g.) as above, reaction being completed on a water-bath (30 min.). The product [7] (0·80 g., 73%) crystallised from aqueous alcohol (1 : 1) as needles, m. p. 98—99° (Found: C, 70·8; H, 6·0. Calc. for $C_{16}H_{16}O_4$: C, 70·6; H, 5·9%), $\nu_{max.}$ 1636 cm.$^{-1}$.

2,3,3′,4,4′,5′-Hexamethoxybenzophenone.[7]—Trimethylgallic acid (10·6 g.) and pyrogallol trimethyl ether (8·4 g.) were treated as above in polyphosphoric acid (from 88 g. of phosphorus pentoxide). The material (16·3 g., 87%) which separated on dilution recrystallised from aqueous ethanol with m. p. 121°, as reported by Perkin and Weizmann [7] (Found: C, 62·9; H, 6·2. Calc. for $C_{19}H_{22}O_7$: C, 62·9; H, 6·1%). It had $\nu_{max.}$ 1650 cm.$^{-1}$.

Reactions of Catechol and its Cyclic Ethers in Polyphosphoric Acid.—(*a*) Methylenedioxybenzene (0·50 g.) dissolved in the acid with a red colour which deepened during 2 hr. of stirring at 20—22°. After dilution in water two polymeric products were separated, one (0·26 g.) by ether-extraction and the other (0·11 g.) by subsequent extraction with benzene. None of the starting material was recovered.

(*b*) A mixture of catechol (13·0 g.) and trimethylgallic acid (25·0 g.) was stirred into polyphosphoric acid (from 200 g. of phosphorus pentoxide) to give a solution initially yellow and deepening to red in 30 min. at 85°. After 40 minutes' heating, the solution was poured into ice-water (400 ml.). The *monoester* (33 g., 91%) separated and crystallised from aqueous ethanol (1 : 1) with m. p. 178—179° (Found: C, 63·1; H, 5·2. $C_{16}H_{16}O_6$ requires C, 63·2; H, 5·3%) and $\nu_{max.}$ 3450b and 1736 cm.$^{-1}$ (ester C=O).

When the experiment was repeated with catechol (11·0 g.) and trimethylgallic acid (42·4 g., 2 equiv.) and the product (35 g.) washed with sodium hydrogen carbonate solution, the product (30 g., 97%) was recrystallised from aqueous alcohol and identified as the monoester obtained previously.

(*c*) Catechol and syringic acid were converted into the *monoester* by method (*b*) on a 0·05-mole scale, a yield of 75% being obtained. The product had m. p. 212° after recrystallisation from 1 : 1 aqueous ethanol (Found: C, 62·0; H, 4·8. $C_{15}H_{14}O_6$ requires C, 62·1; H, 4·9%), $\nu_{max.}$ 3350b and 1725 cm.$^{-1}$ (ester C=O).

(*d*) Diphenylmethylenedioxybenzene [19] (3·0 g.) and trimethylgallic acid (2·32 g.) were stirred into polyphosphoric acid (from 25 g. of phosphorus pentoxide); the temperature of the solution was kept at 85° for 35 min. and pouring into water gave material (4·9 g.) that, recrystallised from aqueous ethanol (1 : 4), had m. p. [and mixed m. p. with the monoester from (*b*)] 176—177° (3 g., 90%) yield; the infrared spectra of the two products were identical.

Reaction of Catechol with Trimethylgallic Acid Catalysed by Boron Trifluoride.—The reagents (0·02 mole) were refluxed for 5 hr. in diethyl ether (40 ml. containing 45% of boron trifluoride), a deep red colour developing. The cold ethereal solution was treated with water (100 ml.), the ether was distilled off, and the hot liquor decanted from an insoluble oil (2 g., 35%) which, crystallised from aqueous alcohol (1 : 1), had m. p. 179°; the mixed m. p. and the infrared

[19] Mason, *J. Amer. Chem. Soc.*, 1944, **66**, 1157.

XUM

spectrum showed that this material was the monoester obtained previously. Methylation of the product (1·0 g.), under the conditions used in preparation of 3,3′,4,4′-tetramethoxybenzophenone, afforded *guaiacol trimethylgallate* (0·70 g.), m. p. 113° (from ethanol) (Found: C, 64·2; H, 5·7. $C_{17}H_{18}O_6$ requires C, 64·1; H, 5·7%). An identical product was obtained on methylation of the monoester prepared as in (*b*) above.

Catechol Bistrimethylgallate: Attempted Fries Rearrangement.—A mixture of catechol (2·5 g.) and trimethylgalloyl chloride (10·5 g.) was kept molten for 2 hr. Evolution of hydrogen chloride having ceased, the melt was cooled and the solid product washed with sodium hydrogen carbonate solution, to yield the diester [14] (11·4 g., 97%) which, recrystallised from benzene–light petroleum (1 : 1; b. p. 60—80°), had m. p. 154° (Found: C, 62·7; H, 5·4. Calc. for $C_{26}H_{26}O_{10}$: C, 62·7; H, 5·3%).

The diester (4·0 g., 0·008) was heated in nitrobenzene (70 ml.) on a steam-bath for 4 hr. with aluminium trichloride (3·5 g.): on cooling, the mixture was acidified with 5N-hydrochloric acid (20 ml.) and steam-distilled. Syringic acid (1·5 g.), m. p. 203°, separated from the aqueous residue and a further quantity (1·3 g., bulk yield 85%) was obtained by ether extraction of the water-insoluble residue. A test with ferric chloride showed that catechol was present in the steam-distillate.

3′,4′,5′-Trihydroxy-2,3,4-trimethoxybenzophenone.—A mixture of gallic acid (4·0 g.) and pyrogallol trimethyl ether (3·95 g.) was stirred into polyphosphoric acid (from 48 g. of phosphorus pentoxide) and the solution kept at 90° for 1 hr., then poured into ice-water (100 ml.). Solid (0·5 g.) separated, a further quantity (2·2 g.) being extracted with ether. These fractions were found to be a mixture of starting materials, in which pyrogallol trimethyl ether predominated. The aqueous liquor was refluxed with 2N-hydrochloric acid (200 ml.) for 2 hr. and extracted with ether (4 × 100 ml.), then evaporation of the dried ($MgSO_4$) extracts afforded the *ketone* (2·7 g., 39%) that crystallised from aqueous ethanol (1 : 1) as needles, m. p. 181—182° (Found: C, 60·1; H, 5·0. $C_{16}H_{16}O_7$ requires C, 60·0; H, 5·0%), $\nu_{max.}$ 3300b and 1663 cm.$^{-1}$ (ketone C=O).

The ketone (0·34 g.) in sodium hydroxide solution (0·18 g. in 15 ml. of water) was heated with dimethyl sulphate (0·5 ml.) on a steam-bath for 30 min. A sample of the precipitate (0·16 g., 83%) crystallised from methanol with m. p. 121—122°, and was identified as 2,3,3′,4,4′,5′-hexamethoxybenzophenone by mixed m. p. and comparison of infrared spectra.

Reaction between Guaiacol and Vanillic Acid.—A mixture of the reagents (0·03 mole) was heated in polyphosphoric acid (from 50 g. of phosphorus pentoxide) for 30 min. at 80°, then poured into ice-water (250 g.). A yellow solid A (3·7 g.) separated, which contained phosphorus and was insoluble in the common organic solvents. Two other fractions were obtained: B (1·45 g.) by ether extraction of the mother liquor; and C (2·3 g.) by ether extraction of the same liquor after 3 hours' heating with 4N-hydrochloric acid on a steam-bath. The three fractions were worked up as follows: (A) Treatment with 2N-sodium hydroxide solution (50 ml.) for 4 hr. on a steam-bath, and extraction with ether, yielded a solid (2·8 g.) which was separated into vanillic acid (1·5 g.) and guaiacol (1·0 g.) by crystallisation from benzene containing 5% of ethanol. Fractions (B) and (C) by crystallisation as above gave vanillic acid (2·2 g.) and guaiacol (1·3 g.). The total recovery of vanillic acid was 74% and of guaiacol 60%; no ketone was detected.

Analyses were by Mrs. P. Charles and Mr. B. T. Saunderson. We thank Mr. G. A. Newman for the measurement of infrared spectra, the Governors of Sir John Cass College for a maintenance grant (to R. C. Denney), and the Department of Scientific and Industrial Research for an equipment grant.

CHEMISTRY DEPARTMENT, SIR JOHN CASS COLLEGE, JEWRY STREET,
ALDGATE, LONDON, E.C.3. [*Received, May 12th*, 1961.]

888. *The Action of Sulphur Monochloride on Aromatic Hydrocarbons.*

By Z. S. Ariyan and L. A. Wiles.

The uncatalysed action of sulphur monochloride on aromatic hydrocarbons has been studied. Many of the more reactive hydrocarbons give di-, tri-, or tetra-sulphides. The chlorodithio-derivative ($R{\cdot}S_2Cl$) * obtained from anthracene is readily converted into a tetrasulphide; while naphthacene gives a di(chlorodithio-derivative). Possible mechanisms of the reactions are discussed.

A variety of products has been reported by different workers as formed by the action of sulphur monochloride, S_2Cl_2, on aromatic hydrocarbons in presence of catalysts such as aluminium, aluminium chloride, and iodine. For example, linear sulphides, thianthrene, and thianthrene polymers have been made from benzene,[1] polymeric sulphides from naphthalene [2,3] and anthracene,[2] and ClS_2-derivatives from naphthalene,[4] anthracene,[5] 1,2-benzanthracene, 3,4-benzopyrene, and 10-methyl-1,2-benzanthracene.[6] Some of the results are so unusual as to merit further investigation, and as a whole the work has not been logically developed. This paper describes the reaction of sulphur monochloride on aromatic hydrocarbons, usually at room temperature, with an inert solvent, and without a catalyst. The annexed Table lists the compounds and their products.

Hydrocarbon	Product	Hydrocarbon	Product
$C_6H_3Me_3$, 1,2,4-	R_2S_3	Naphthalene	$(RS)_x$
1,3,5-	R_2S_3, R_2S_4	Anthracene	RS_2Cl, R_2S_4
$C_6H_2Me_4$, 1,2,3,5-	R_2S_3, R_2S_4	Naphthacene	$X(S_2Cl)_2$
1,2,4,5-	R_2S_4		
C_6HMe_5	R_2S_3		

There was no reaction, with benzene, toluene or the xylenes, or with t-butylbenzene, di- and tri-phenylmethane, triphenylbenzene, fluorene, phenanthrene, pyrene, or chrysene under our conditions. Activation of the benzene nucleus by three or more methyl groups is sufficient.

The products listed were readily isolated from the reaction mixture but it is not claimed that they were the sole products; indeed simultaneous formation of mono- and poly-sulphides in such reactions has often been observed.[7]

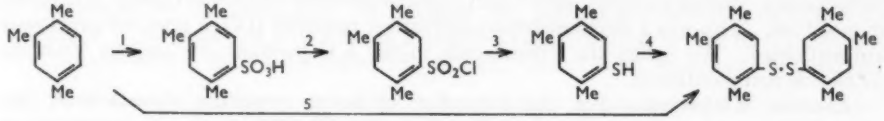
The di-(2,4,5-trimethylphenyl) disulphide obtained from 1,2,4-trimethylbenzene and the related thiol are inadequately identified in the literature. Cohen and Skirrow [8] obtained a thiol, m. p. 87—90°, which they believed to be identical with a compound, m. p. 86—87°, isolated by Beilstein and Kögler.[9] Radloff [10] gave m. p. 85° for this compound, and by its oxidation prepared a disulphide, m. p. 115°; analytical data for these compounds are missing or incomplete. The thiol, m. p. 92°, and disulphide, m. p. 89°, have now been synthesized from 1,2,4-trimethylbenzene by the routes illustrated. The

* Formerly known as dithiochlorides.

[1] Schmidt, *Ber.*, 1878, **11**, 1168; Damanski and Kostic, *Bull. Soc. chim. Beograd*, 1948, **13**, 209.
[2] Damanski and Kostic, *Bull. Soc. chim. Beograd*, 1947, **12**, 243.
[3] Damanski and Binenfeld, *Compt. rend.*, 1959, **249**, 1678; *Bull. Soc. chim. France*, 1961, 679.
[4] Airan and Shah, *J. Indian Chem. Soc.*, 1945, **22**, 359.
[5] Lippmann and Pollak, *Ber.*, 1901, **34**, 2767.
[6] Wood and Fieser, *J. Amer. Chem. Soc.*, 1940, **62**, 2674.
[7] Wieland, Weiberg, Fischer, and Hörlein, *Annalen*, 1954, **587**, 146; Roberts, Wiles, and Kent, *J.*, 1932, 1792; Ariyan and Wiles, unpublished work.
[8] Cohen and Skirrow, *J.*, 1899, **75**, 887.
[9] Beilstein and Kögler, *Annalen*, 1866, **137**, 317.
[10] Radloff, *Ber.*, 1878, **11**, 32.

XUM

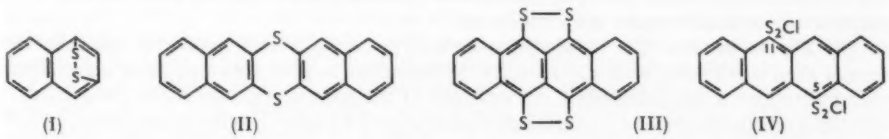
disulphides obtained by the two methods were identical. The thiol was readily distinguished by its solubility in alkali and its infrared spectrum (SH stretching band at 2550 cm.$^{-1}$).



Reagents: 1, H_2SO_4. 2, PCl_5 + Na salt. 3, Zn–H_2SO_4. 4, $FeCl_3$. 5, S_2Cl_2.

The ready formation of a trisulphide from pentamethylbenzene shows the absence of steric effects. It has been considered [11] that steric hindrance in forming polysulphides is only encountered when the groups concerned are larger than isopropyl or phenyl. This statement must, however, be modified when the approach of a sulphur monochloride molecule to a hydrogen atom is involved in forming sulphides from hydrocarbons. Thus 1,3,5-triphenylbenzene in which there is steric repulsion between hydrogen atoms [12] did not react with sulphur monochloride in our uncatalysed reaction; di- and tri-phenylmethane, both non-planar, were also unreactive, though the former with an aluminium–mercury catalyst gives dibenzylthianthrene.[13]

Naphthalene reacts with sulphur monochloride under many different conditions. Heating with zinc chloride gave a resin considered to be a mixture of naphthyl sulphides and polysulphides.[14] With a trace of bismuth chloride a ClS_2-derivative has been reported,[4] and in acetic acid at 100° without a catalyst a disulphide (I) [15] (no molecular weight was published for this compound) was obtained.



(I) (II) (III) (IV)

The dibenzothianthrene (II) is said to have been obtained from naphthalene with aluminium as catalyst but again no molecular weight was given.[2] Later work [3] yielded two isomeric polymeric disulphides.

We failed to obtain the ClS_2-derivative isolated by Airan and Shah [4] under their conditions and also with modifications. The products were always polymeric sulphides of molecular weight *ca.* 550, probably formed from an intermediate ClS_2-derivative. Our experience is that such derivatives are readily hydrolysed, and it is difficult to understand how recrystallisation of this compound from hydroxylic solvents could have been effected by the Indian workers.

Friedländer and Simon [16] obtained 9-chlorodithioanthracene from anthracene and sulphur monochloride. This compound, stirred in ethereal solution in the dark, has now given the 9-anthryl tetrasulphide, m. p. 190° (*M* 460), a type of reaction not hitherto observed.

Shingte, Rege, Pishavikar, and Shah [15] treated anthracene and sulphur monochloride in glacial acetic acid. They reported a disulphide, m. p. 180° (no molecular weight given), which they considered to be 9,10-epidithioanthracene, but other attempts [17] to prepare this disulphide failed and the product of m. p. 180° was probably our tetrasulphide.

[11] Pearson, Caine, and Field, *J. Org. Chem.*, 1960, **25**, 867.
[12] Pauling, "The Nature of the Chemical Bond," Oxford Univ. Press, 3rd edn., 1960, p. 293.
[13] Rây, *J.*, 1921, **119**, 1959.
[14] Signaigo, U.S.P. 2,402,685/1946.
[15] Shingte, Rege, Pishavikar, and Shah, *J. Univ., Bombay*, 1952, **21**, 28.
[16] Friedländer and Simon, *Ber.*, 1922, **55**, 3969.
[17] Hiyama, Ito, and Noguchi, *J. Chem. Soc. Japan*, 1949, **52**, 252.

Marschalk and his co-workers [18] treated naphthacene with sulphur monochloride in 1,2,4-trichlorobenzene at 125°. 5,11-Dichloronaphthacene was first formed and this was then converted into the tetrasulphide (III). We found that this reaction, at ordinary temperature, without a solvent, gave a red, granular material which was rapidly hydrolysed in moist air. This was a di(chlorodithio)-derivative, probably (IV), a type not previously authenticated. We assign the substituents to the 5,11-positions by analogy with the dichloride just mentioned.

Reaction Mechanisms.—For the formation of linear sulphides, thianthrenes, and chlorodithio-compounds by the action of sulphur monochloride on aromatic hydrocarbons there are three possible explanations.

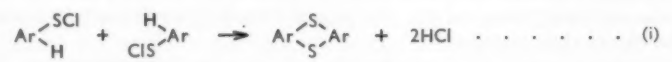
(i) The conversion of sulphur monochloride into other sulphur halides, and subsequent reaction of these with the aromatic compound. Many different equilibria involving sulphur monochloride have been postulated, *e.g.*:

$$S_2Cl_2 \rightleftharpoons SCl_2 + S$$
$$S_2Cl_2 + S \rightleftharpoons S_3Cl_2$$
$$S_2Cl_2 + SCl_2 \rightleftharpoons S_3Cl_4$$

Patrick and Hackerman [19] found that the molecular weight of dilute solutions of sulphur monochloride changed with time, temperature, nature of the solvent, and concentration. Spong [20] showed the density to be altered if the compound is heated at 100° or irradiated by ultraviolet light. Many sulphur chlorides (chlorosulphanes) have now been characterised by Fehér and his co-workers,[21] but the reactions with hydrocarbons have not been studied. The existence of these compounds as intermediates could explain the production of mono- and poly-sulphides. Monosulphides did not react further with sulphur monochloride under our conditions.

(ii) The formation of a chlorodithio-derivative ($R{\cdot}S_2Cl$) and hydrogen chloride, the former then condensing with the aromatic hydrocarbon to give a disulphide or eliminating chlorine to give a tetrasulphide. An example of the former reaction is the condensation of *o*-(chlorodithio)nitrobenzene with anthracene to give 9-anthryl *o*-nitrophenyl disulphide.[22] We have discovered one of the latter in conversion of 9-chlorodithioanthracene into di-9-anthryl tetrasulphide in ethereal suspension in the dark.

(iii) The formation of a sulphenyl chloride (RSCl) by homolytic or heterolytic fission of sulphur monochloride. The sulphenyl chloride could then condense with an aromatic hydrocarbon to give a monosulphide or eliminate chlorine to give a disulphide. The former of these reactions is exemplified by the Friedel–Crafts condensations of 2,4-dinitrobenzenesulphenyl chloride with a series of hydrocarbons,[23] the latter by the rapid



(i)

conversion of naphthalene-2-sulphenyl chloride into the disulphide in dry air.[24] Equally thianthrenes could result from sulphenyl chlorides (see i), suggested by Fries [25] though he could not obtain them in this way. During the present work we have had indications that thianthrene and thianthrene polymers can be obtained from benzenesulphenyl chloride but no sulphenyl chloride was obtained by the direct use of sulphur monochloride.

[18] Marschalk and Stumm, *Bull. Soc. chim. France*, 1948, 418; Clar and Marschalk, *ibid.*, 1950, 433.
[19] Patrick and Hackerman, *J. Phys. Chem.*, 1936, **40**, 679.
[20] Spong, *J.*, 1934, 485.
[21] Fehér, *Chem. Soc. Special Publ.*, No. 12, 1958, 305.
[22] Harris, Ph.D. Thesis, Univ. of Pennsylvania, 1953.
[23] Buess and Kharasch, *J. Amer. Chem. Soc.*, 1950, **72**, 3529.
[24] Zincke and Eismayer, *Ber.*, 1918, **51**, 751.
[25] Fries, *Ber.*, 1912, **45**, 2965.

If a chlorodithio-derivative and a sulphenyl chloride were formed simultaneously their interactions would explain the variety of products which arise.

Of the three mechanisms, only the formation of a chlorodithio-derivative by reaction of an aromatic hydrocarbon (*e.g.*, anthracene) and sulphur monochloride is definitely established. Although the formation of a sulphenyl chloride in this type of reaction has never been observed, there is no reason why sulphur monochloride should not be polarised as $Cl-\overset{\delta+}{S}-\overset{\delta-}{S}-Cl$ and then undergo heterolysis. Bateman, Moore, and Porter [26] have concluded that homolysis of disulphide bonds is restricted to reactions involving photo-initiation, high temperature, or attack by other radicals. In favour of heterolytic fission are the catalysed reactions of aromatic hydrocarbons and sulphur monochloride, and it is noteworthy that the hydrocarbons which we find to react most readily with this reagent are (with the exception of durene) those which couple with reactive diazonium salts.

Experimental

General Procedure.—Commercial sulphur monochloride (500 g.) was purified by distillation from sulphur (20 g.) and charcoal (5 g.). The fraction of b. p. 135—137° was stored in a dark bottle in a refrigerator. To the redistilled hydrocarbon in sodium-dried " AnalaR " ether was added the calculated quantity of sulphur monochloride in ether. The mixture was left in daylight (usually for some days) until a sample did not deposit sulphur when treated with water. It was then shaken with sodium carbonate solution, the ethereal layer was dried, the ether removed, and the oily product steam-distilled. The residue was then again extracted with ether, dried, and recovered. The compound usually crystallised. In some cases the oil was chromatographed on an alumina column.

Di-(2,4,5-trimethylphenyl) Disulphide.—1,2,4-Trimethylbenzene (22 g., 0·2 mole) and sulphur monochloride (13·5 g., 0·1 mole) were left in ether (200 ml.) for 5 days. Repeated recrystallisation from light petroleum (b. p. 40—60°) gave a pale yellow solid, m. p. 88—89° (64%) (Found: C, 71·3; H, 7·7; S, 21·2. $C_{18}H_{22}S_2$ requires C, 71·5; H, 7·3; S, 21·2%).

2,4,5-Trimethylbenzenethiol.—2,4,5-Trimethylbenzenesulphonyl chloride [27] (10·2 g., 0·05 mole) was added in small portions with stirring during ½ hr. to ice (72 g.) and 98% sulphuric acid (13 ml.), and the mixture kept at between −5° and 0° during addition of zinc dust (12 g.), then was refluxed for 4—6 hr. The *thiol* was removed in steam and recrystallised from alcohol as plates, m. p. 92° (62%) (Found: C, 70·6; H, 7·8; S, 21·4. $C_9H_{12}S$ requires C, 71·0; H, 7·9; S, 21·1%).

40% Aqueous ferric chloride (10 ml.) was added to the thiol (1·5 g., 0·01 mole) in acetic acid (5 ml.), and the mixture was boiled. A yellow compound, insoluble in alkali, separated after a short time. Recrystallised from alcohol it had m. p. 89° alone or mixed with the compound obtained by reaction of 1,2,4-trimethylbenzene and sulphur monochloride as above.

Di-(2,4,6-trimethylphenyl) Tetra- and Di-sulphide.—A mixture of 1,3,5-trimethylbenzene (22 g., 0·2 mole) and sulphur monochloride (13·5 g., 0·1 mole) in ether (200 ml.) was left for 4 days. Treatment according to the general procedure and recrystallisation from light petroleum (b. p. 40—60°) gave a yellow *tetrasulphide*, m. p. 100° (42%) [Found: C, 59·6; H, 6·1; S, 34·4%; *M* (cryoscopic in C_6H_6), 360. $C_{18}H_{22}S_4$ requires C, 59·0; H, 6·1; S, 34·9%; *M*, 367]. The petroleum filtrate, on evaporation, gave the disulphide as an orange oil which crystallised. Repeated recrystallisation from light petroleum gave yellow needles, m. p. 125° (19%) in agreement with Holtmeyer [28] (Found: C, 72·0; H, 7·7; S, 20·9. Calc. for $C_{18}H_{22}S_2$: C, 71·5; H, 7·3; S, 21·2%).

Di-(2,3,4,6-tetramethylphenyl) Tri- and Tetra-sulphide.—1,2,3,5-Tetramethylbenzene (1·3 g., 0·01 mole) and sulphur monochloride (1·3 g., 0·01 mole) were left in ether (20 ml.) for 1 week. The usual treatment gave the *tetrasulphide* as a yellow oil (43%) which boiled with decomposition under reduced pressure (Found: C, 60·0; H, 6·5; S, 33·2. $C_{20}H_{26}S_4$ requires C, 60·9; H, 6·6; S, 32·5%).

This reaction, but at 100° for 2 hr., gave the *trisulphide* as a light yellow oil (62%) which

[26] Bateman, Moore, and Porter, *J.*, 1958, 2866.
[27] Schreinemakers, *Rec. Trav. chim.*, 1897, **16**, 411.
[28] Holtmeyer, *Z. Chem.*, 1867, 688.

boiled with decomposition under reduced pressure (Found: C, 65·8; H, 6·9; S, 27·2. $C_{20}H_{26}S_3$ requires C, 66·3; H, 7·2; S, 26·5%).

Di-(2,3,5,6-tetramethylphenyl) Tetrasulphide.—1,2,4,5-Tetramethylbenzene (13·4 g., 0·1 mole) and sulphur monochloride (13·5 g., 0·1 mole) were left in ether (200 ml.) for 5 days. The usual procedure gave, after repeated recrystallisation from light petroleum–acetone, the pale-yellow *tetrasulphide*, m. p. 165° (55%) (Found: C, 61·3; H, 6·7; S, 32·0. $C_{20}H_{26}S_4$ requires C, 60·9; H, 6·6; S, 32·5%).

Di(pentamethylphenyl) Trisulphide.—Pentamethylbenzene (7·4 g., 0·05 mole) and sulphur monochloride (6·25 g., 0·05 mole) were left in ether for 1 week. The precipitated *trisulphide*, when recrystallised several times from benzene, was pale yellow and had m. p. 189° (43%) (Found: C, 67·9; H, 7·6; S, 24·3. $C_{22}H_{30}S_3$ requires C, 67·6; H, 7·7; S, 24·6%).

Naphthyl Polysulphide.—Naphthalene (12·8 g., 0·1 mole) and sulphur monochloride (13·5 g., 0·1 mole) were left in ether for 10 days. A yellow, amorphous solid containing C, H, and S was isolated [*M* (Rast), *ca.* 550].

9-Chlorodithioanthracene.—Sulphur monochloride (13·5 g., 0·1 mole) was poured on anthracene (8·9 g., 0·05 mole). After a short time vigorous evolution of hydrogen chloride occurred. When this was complete red needles separated. This derivative, when washed with ether and then light petroleum, had m. p. 117—118° (90%) (Found: C, 60·3; H, 3·0; Cl, 12·4; S. 22·7. Calc. for $C_{14}H_9ClS_2$: C, 60·7; H, 3·3; Cl, 12·8; S, 23·2%).

Di-9-anthryl Tetrasulphide.—The foregoing derivative (13·8 g., 0·05 mole) was suspended in ether (200 ml.) and stirred in the dark for one day. Removal of the ether and recrystallisation from benzene gave the tetrasulphide as orange plates, m. p. 190° (64%) in agreement with Cooke, Heilbron, and Walker [29] [Found: C, 68·8; H, 3·5; S, 26·4%; *M* (cryoscopic in C_6H_6), 460. Calc. for $C_{28}H_{18}S_4$: C, 69·7; H, 3·8; S, 26·6%; *M*, 483].

5,11-Di(chlorodithio)naphthacene.—Sulphur monochloride (4·1 g., 0·03 mole) was poured on naphthacene (2·2 g., 0·01 mole). Vigorous evolution of hydrogen chloride occurred and the reaction was controlled by adding a few ml. of hexane. A red oily *derivative* separated and, triturated with light petroleum, gave a granular red solid (70%) which was hydrolysed rapidly in moist air and melted with decomposition (Found: C, 51·3; H, 2·9; Cl, 16·5; S, 28·9. $C_{18}H_{10}Cl_2S_4$ requires C, 50·8; H, 2·4; Cl, 16·7; S, 30·1%).

We acknowledge generous gifts of isodurene from the British Petroleum Co., Ltd., and from Esso Research Ltd.

Department of Chemistry and Metallurgy, Royal Military College of Science, Shrivenham, Swindon, Wilts. [*Received, May 19th,* 1961.]

[29] Cooke, Heilbron, and Walker, *J.*, 1925, **127**, 2250.

---

889. *The Action of Aluminium Chloride on Some o-Alkylbenzenesulphonic Acids and o-Alkyldiphenyl Sulphones.*

By G. Holt and B. Pagdin.

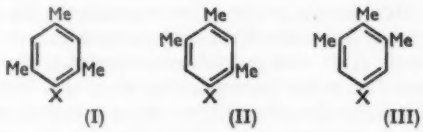
o-Alkylbenzenesulphonic acids and *o*-alkyldiphenyl sulphones isomerise when fused with aluminium chloride, to give products which are frequently not readily available by other means. Conversion of 2,4,6-trimethylbenzenesulphonic acid into the 3,4,5-isomer followed by desulphonation is a simple procedure for the preparation of 1,2,3-trimethylbenzene. In the sulphone series rearranged products were obtained only when two *o*-methyl groups were present but one sufficed in the sulphonic acids. The greater mobility of the ethyl group is demonstrated by the rearrangement of both sulphonic acids and of sulphones containing one such *ortho*-substituent.

The literature contains no references to the action of aluminium chloride on alkylbenzenesulphonic acids or on alkylated diphenyl sulphones. Baddeley [1] has shown that *o*-alkylated aromatic ketones undergo a variety of irreversible isomerisations when fused with aluminium chloride to provide benzene derivatives which in some instances are not readily

[1] Baddeley, *Quart. Rev.*, 1954, **8**, 355.

available by other means because of the unusual orientation of the substituents. For example, 3,4,5-trimethylacetophenone has been obtained from its readily available 2,4,6-isomer. Migration of alkyl groups in alkylbenzenesulphonic acids (the Jacobsen reaction [2]) occurs only when the aromatic ring has at least four alkyl substituents. We now report the migration of alkyl groups in the aromatic sulphonic acids and sulphones in which the aromatic ring has three and in some instances only two alkyl substituents.

With aluminium chloride at 200° 2,4,6- and 2,4,5-trimethyldiphenyl sulphone (I and II; X = SO_2Ph) afforded the 3,4,5-isomer (III; X = SO_2Ph) in substantially the same yield (26%):



The greater influence of two *o*-alkyl groups than of one on these reactions is illustrated by the observation that 2,4,6-trimethyldiphenyl sulphone yields the 2,4,5-isomer at 140° (65%) and that even after prolonged heating at this temperature none of the 3,4,5-isomer could be isolated although the latter is formed at 200°. Even at this higher temperature, 2-methyl- and 2,5-dimethyl-diphenyl sulphone failed to rearrange. In view of the recognised greater mobility of ethyl groups 2,5-diethyldiphenyl sulphone was fused with aluminium chloride at 150°: it gave 3,5-diethyldiphenyl sulphone in 45% yield.

Fusion of the corresponding sodium alkylbenzenesulphonates with aluminium chloride provided somewhat similar results but, in general, isomerisation proceeded more readily. The results are shown in the Table.

Alkylbenzenesulphonic acid	Fusion temp.	Reaction time (hr.)	Rearrangement product
2,4,6-Me_3 (I; X = SO_3H)	140°	5	2,4,5-Me_3 (73%) *
,, ,, ...	200	10	3,4,5-Me_3 (60%)
2,4,5-Me_3 (II; X = SO_3H)	200	10	3,4,5-Me_3 (16%)
2,5-Me_2	200	12·5	3,5-Me_2 (59%)
2,5-Et_2	150	5	3,5-Et_2 (30%)
2,4,6-Et_3	150	5	3,5-Et_2 (30%)

* Based on 1,2,4-trimethylbenzene obtained by hydrolysis of the sulphonic acid.

The isolation of 3,5-dimethylbenzenesulphonic acid when the 2,5-isomer is fused with aluminium chloride at 200° demonstrates the greater mobility of alkyl groups in sulphonic acids than in sulphones since no rearranged product was isolated from 2,5-dimethyldiphenyl sulphone under similar conditions. In the Jacobsen reaction both intramolecular and intermolecular migration of alkyl groups is encountered. No products of intermolecular alkyl group migration have been isolated in the present work although it is possible that these were formed in small amounts and remained undetected. That alkyl groups can be lost in the aluminium chloride-catalysed isomerisation of sulphonic acids is shown by the isolation of 3,5-diethylbenzenesulphonic acid when 2,4,6-triethylbenzenesulphonic acid is fused at 150°. Presumably the two *o*-alkyl groups migrate to the corresponding *meta*-positions and an ethyl group is eliminated from the first formed 3,4,5-isomer.

In view of the experimental difficulties involved in the isolation of the sulphonic acids the yields claimed are conservative. A more accurate assessment of the yield was obtained in some instances by hydrolysis of the products and isolation and identification of the resulting benzene homologues: thus fractional hydrolysis of the sulphonic acids

[2] "Organic Reactions," Adams, New York, John Wiley & Sons Inc., 1942, Vol. I, Compilation of References, p. 370.

given by 2,4,6-trimethylbenzenesulphonic acid when heated with aluminium chloride at 140° for 5 hours gave mesitylene (2%) and 1,2,4-trimethylbenzene (73%), whereas the corresponding 2,4,5-trimethylbenzenesulphonic acid was isolated, as the sulphonamide, in only 56% yield. This hydrolysis procedure was not always so satisfactory; *e.g.*, fractional hydrolysis of the product obtained when the above fusion was carried out at 200° gave 1,2,3-trimethylbenzene in only 30% yield although its sulphonic acid, as the sulphonyl chloride, was isolated in 60% yield. This difference is a consequence of the difficulty of hydrolysing benzenesulphonic acids which do not have an *o*-alkyl substituent.

The results outlined above make it clear that: (i) the migration of one *o*-alkyl group is facilitated by a second alkyl group in the other *o*-position; (ii) an ethyl group is more mobile than a methyl group; (iii) isomerisation of a sulphone is more difficult than that of the corresponding sulphonic acid; and (iv) isomerisation of both sulphones and sulphonic acids is more difficult than that of the corresponding alkyl aryl ketones.[3,4]

Several of the isomerisations described above make available new sulphonic acids and sulphones. An example is 3,4,5-trimethylbenzenesulphonic acid, obtained from the readily available 2,4,6-isomer. Sulphonation of 1,2,3-trimethylbenzene provides, of course, 2,3,4-trimethylbenzenesulphonic acid.[5] Again, the preparation of 3,5-dimethylbenzenesulphonic acid by isomerisation of the 2,5-isomer is much simpler than procedures described previously.[6]

Experimental

Fusion of Sulphones with Aluminium Chloride.—The sulphone (1 part) was added in small portions to a stirred melt of aluminium chloride (10 parts) and sodium chloride (1 part). After being heated for the time and at the temperature indicated below, the melt was cooled to 120° and poured cautiously with stirring into ice and dilute hydrochloric acid. The resulting mixture was extracted with ethylene dichloride, and the extracts were washed with water and with sodium hydroxide solution and dried (K_2CO_3). The solvent was distilled off and the residue purified as described below.

(*a*) 2,4,6-Trimethyldiphenyl sulphone [7] (2 g.) on fusion at 140° for 9 hr. gave a pale brown solid (1·6 g.) which, on crystallisation from ethanol, provided fern-like crystals (1·3 g., 65%) of 2,4,5-trimethyldiphenyl sulphone,[7] m. p. and mixed m. p. 136—137°. Attempts to effect a more efficient separation by chromatography on alumina were unsuccessful.

(*b*) 2,4,5-Trimethyldiphenyl sulphone (5 g.) on fusion at 200° for 10 hr. gave a crude product (4·25 g.; m. p. 104—110°) which on fractional crystallisation from ethanol yielded 3,4,5-trimethyldiphenyl sulphone [7] (1·3 g., 26%), m. p. and mixed m. p. 159—161°, and unchanged starting material (0·3 g.). The same sulphone on fusion in a sealed tube at 250° for 5 hr. yielded only carbonaceous material and intractable tar.

(*c*) 2,5-Dimethyldiphenyl sulphone [7] (2 g.) on fusion at 200° for 10 hr. gave a pale brown oil (1·6 g.), fractional crystallisation of which from light petroleum (b. p. 60—80°) afforded only unchanged starting material (0·6 g.), m. p. and mixed m. p. 108—110°.

(*d*) 2-Methyldiphenyl sulphone [7] (5 g.) on fusion at 200° for 48 hr. gave a black semi-solid mass (4·2 g.), extraction of which with light petroleum (b. p. 0—40°) yielded only unchanged starting material (1·3 g.), m. p. and mixed m. p. 79—80°.

(*e*) 2,5-Diethyldiphenyl sulphone [7] (2 g.), m. p. 84—86°, on fusion at 150° for 5 hr. gave a sticky product which was extracted with light petroleum (b. p. 40—60°). The extract, on cooling and partial removal of the solvent, yielded a solid which on crystallisation from benzene–light petroleum gave 3,5-*diethyldiphenyl sulphone* (0·9 g., 45%), m. p. 84—86° (Found: C, 70·2; H, 6·6; S, 11·7. $C_{16}H_{18}O_2S$ requires C, 70·1; H, 6·6; S, 11·7%). This depressed the m. p. of the starting material and yielded on oxidation by nitric acid an acid, m. p. 236°, identical (mixed m. p.) with the acid similarly obtained by oxidation of 3,5-dimethyldiphenyl sulphone.

Fusion of Sodium Sulphonates with Aluminium Chloride.—The sodium sulphonate (1 part) was added in small portions to a stirred melt of aluminium chloride (10 parts) and sodium

[3] Baddeley, *J.*, 1944, 232.
[4] Varma, Ph.D. Thesis, Manchester, 1955.
[5] Auwers and Weiners, *Ber.*, 1925, **58**, 2815.
[6] Moschner, *Ber.*, 1901, **34**, 1260.
[7] Holt and Pagdin, *J.*, 1960, 2508.

XUM

chloride (1 part). After being heated for the time and at the temperature indicated below the melt was cooled to 120° and poured cautiously with stirring into a mixture of ice and water. The resulting mixture was filtered to remove carbonaceous material, heated to boiling, and rendered just neutral to litmus by the addition of sodium hydroxide solution. The precipitated aluminium hydroxide was coagulated by further heating, filtered off, and washed with hot water. The combined filtrate and washings were evaporated and the dry mixture of sodium sulphonates and sodium chloride was treated with phosphorus pentachloride and phosphorus oxychloride. The crude sulphonyl chloride was treated as indicated below. Alternatively, the mixture of sulphonic acids was subjected to fractional hydrolysis and the resulting hydrocarbons were collected and characterised.

(*a*) Sodium 2,4,6-trimethylbenzenesulphonate (5 g.) after reaction at 140° for 5 hr. and subsequent working up provided a sulphonyl chloride (3·84 g., 78%, m. p. 47—58°). The latter yielded a mixture of sulphonamides from which 2,4,5-trimethylbenzenesulphonamide (56%; m. p. 181°) was isolated by virtue of the insolubility of its sodium salt in water. The mixture of sulphonic acids resulting from a similar fusion of sulphonate (10 g.) was subjected to fractional desulphonation. Hydrolysis of the small amount of unchanged 2,4,6-trimethylbenzenesulphonic acid by the procedure of Smith and Cass [8] provided 1,3,5-trimethylbenzene (0·15 g., 2%; b. p. 160—164°) (sulphonamide,[9] m. p. and mixed m. p. 144°). The residual 2,4,5-trimethylbenzenesulphonic acid was hydrolysed by passing steam through its solution in 50% sulphuric acid at 140°. 1,2,4-Trimethylbenzene (3·9 g., 73%; b. p. 166—169°, n_D^{20} 1·5035) (sulphonamide m. p. and mixed m. p. 181°) was isolated from the distillate. No further hydrocarbon could be isolated even though the temperature of the mixture was raised to 200° whilst superheated steam was passed through it.

Isomerisation of sodium 2,4,6-trimethylbenzenesulphonate at 200° for 10 hr. gave sodium 3,4,5-trimethylbenzenesulphonate, isolated as the *sulphonyl chloride* (60%) which separated from light petroleum (b. p. 0—40°) in parallelepipeds, m. p. 119—121° (Found: C, 49·2; H, 5·3. $C_9H_{11}ClO_2S$ requires C, 49·4; H, 5·3%). The *sulphonamide* separated from ethanol in needles, m. p. and mixed m. p. 171—173° (Found: C, 54·6; H, 6·4; N, 7·3. $C_9H_{13}NO_2S$ requires C, 54·3; H, 6·5; N, 7·0%). When fused with potassium hydroxide according to Hartmann's method [10] the above sulphonyl chloride gave 3,4,5-trimethylphenol,[11] m. p. and mixed m. p. 102—104°.

(*b*) Sodium 2,4,5-trimethylbenzenesulphonate, after reaction at 200° for 15 hr., gave a mixture of sodium salts and thence an oily sulphonyl chloride (10 g., 51%). The solid (3 g.) obtained by triturating this oil with light petroleum yielded a sulphonamide which did not depress the m. p. (171—173°) of 3,4,5-trimethylbenzenesulphonamide. The oily portion of the sulphonyl chloride on treatment with ammonia provided a mixture of sulphonamides which could not be separated. The mixture of sulphonic acids produced in this reaction was subjected to fractional hydrolysis with phosphoric acid as described below for the 2,4,6-isomer. 1,2,4-Trimethylbenzene (8·5%) and 1,2,3-trimethylbenzene (16·5%) were obtained and characterised as their sulphonamides.

(*c*) Sodium 2,5-dimethylbenzenesulphonate (20 g.), after reaction at 200° for 12 hr., gave a sulphonyl chloride (11·7 g., 59%; m. p. 82—88°) which on crystallisation from light petroleum (b. p. 60—80°) yielded 3,5-dimethylbenzenesulphonyl chloride, m. p. 91—92° (Found: C, 47·0; H, 4·3. Calc. for $C_8H_9ClO_2S$: C, 46·9; H, 4·4%). The sulphonamide (Found: C, 52·1; H, 6·1; N, 7·4. Calc. for $C_8H_{11}NO_2S$: C, 51·9; H, 6·0; N, 7·6%) prepared from this chloride did not depress the m. p. (135·5°) of authentic 3,5-dimethylbenzenesulphonamide.[6] The sulphonyl chloride, on fusion with potassium hydroxide, provided 1,3,5-xylenol,[12] m. p. and mixed m. p. 64°, which was further characterised as its toluene-*p*-sulphonate, m. p. 84°.

(*d*) Sodium 2,5-diethylbenzenesulphonate (20 g.), after reaction at 150° for 5 hr., gave a dark brown oily sulphonyl chloride (14·4 g., 69%). The latter (2 g.) afforded *3,5-diethylbenzenesulphonamide* (0·55 g., 30%), m. p. 93° (Found: C, 56·3; H, 7·0; N, 6·6; S, 14·5. $C_{10}H_{15}NO_2S$ requires C, 56·5; H, 7·1; N, 6·6; S, 15·0%). No identifiable products were obtained by crystallisation or chromatography of the material contained in the benzene–light petroleum

[8] Smith and Cass, *J. Amer. Chem. Soc.*, 1932, **54**, 1603.
[9] Gibson, *J.*, 1920, **117**, 953.
[10] Hartmann, *Org. Synth.*, 1923, **3**, 37.
[11] Baddeley, *J.*, 1943, 527.
[12] Ipatiew and Petrow, *Ber.*, 1927, **60**, 1963.

mother liquor from the crystallisation of this sulphonamide. Attempts to purify the crude sulphonyl chloride by fractional distillation were unsuccessful.

(*e*) Sodium 2,4,6-triethylbenzenesulphonate (5 g.), after reaction at 150° for 5 hr., gave an oily sulphonyl chloride (3·2 g., 65%) which, with ammonia, provided an oily sulphonamide (3 g.). The latter on trituration with ethanol yielded a sticky solid (0·5 g.) which was extracted with light petroleum (b. p. 60—80°); the extracts slowly deposited a white solid (0·33 g.), m. p. 89—91°. Recrystallisation from light petroleum (b. p. 60—80°) gave 3,5-diethylbenzenesulphonamide (0·3 g.) as needles, m. p. 91—92° (Found: C, 56·1; H, 7·0; S, 15·0%). This material did not depress the m. p. (91—92°) of the 3,5-diethylbenzenesulphonamide obtained in the previous experiment. When the fusion was carried out at 120° for 1·5 hr. the product appeared to be extremely complex and no solid sulphonamide was obtained.

Preparation of 1,2,3-*Trimethylbenzene from* 2,4,6-*Trimethylbenzenesulphonic Acid.*—Sodium 2,4,6-trimethylbenzenesulphonate (50 g.) was fused with aluminium chloride (200 g.) and sodium chloride (16 g.) at 200° for 10 hr. The cooled melt was decomposed by water (2 l.) and after the addition of phosphoric acid (1 l.; *d* 1·750) the mixture was heated whilst steam was passed through it. When the temperature inside the flask reached 140° hydrocarbon began to pass over with the steam and distillation was continued at this temperature until oily drops no longer passed over. The distillate was neutralised and extracted with chloroform, and the dried (K_2CO_3) extracts were concentrated. Distillation of the residue provided 1,2,4-trimethylbenzene (2·3 g., 8·5%; b. p. 164—165°) (sulphonamide, m. p. and mixed m. p. 179—181°). The temperature inside the flask was raised until, at 170°, oil again appeared in the steam-distillate. The oil was removed from the distillate by extraction with chloroform, and the residue obtained on concentration of the dried chloroform extracts was distilled to provide 1,2,3-trimethylbenzene (8 g., 30%; b. p. 168—172°) (sulphonamide,[8] m. p. and mixed m. p. 194—196°).

Alternative Syntheses.—3,5-*Dimethylbenzenesulphonamide.* The neutral sulphate of 2,4-dimethylaniline was heated under reduced pressure,[13] providing 2-amino-3,5-dimethylbenzenesulphonic acid (56%). The latter on deamination [14] provided 3,5-dimethylbenzenesulphonic acid which was converted into the sulphonamide (m. p. 135·5°) in the usual manner.

3,4,5-*Trimethylbenzenesulphonamide.* 3,4,5-Trimethylacetophenone oxime [8] on Beckmann rearrangement with polyphosphoric acid afforded 3,4,5-trimethylacetanilide in virtually quantitative yield. Hydrolysis of this acetyl derivative gave 5-amino-1,2,3-trimethylbenzene [15] (90%) which was diazotised and converted [16] into the corresponding sulphinic acid (23%). Treatment of the latter with chlorine and ammonia afforded the required sulphonamide (60%), m. p. 169—172° (from ethanol) (Found: C, 54·6; H, 6·4; N, 7·3. Calc. for $C_9H_{13}NO_2S$: C, 54·3; H, 6·5; N, 7·0%).

Separation of 2,4,5- *and* 2,4,6-*Trimethylbenzenesulphonamide.*—To an intimate mixture of 2,4,6-trimethylbenzenesulphonamide (1 g.) and 2,4,5-trimethylbenzenesulphonamide (1 g.) was added 2N-sodium hydroxide (10 ml.). The sodium 2,4,6-trimethylbenzenesulphonamide was dissolved by warming the stirred mixture to 60°. The cooled (10°) suspension was filtered, the solid was washed with a few drops of 2N-sodium hydroxide, and the combined filtrate and washings (A) were collected. The solid (1·13 g.) was taken up in the minimum volume of hot water and acidified with 2N-sulphuric acid. The sulphonamide which crystallised from the cooled solution was separated, washed with cold water until sulphate-free, and dried (0·85 g., 85%; m. p. 175—178°). One recrystallisation from aqueous ethanol gave 2,4,5-trimethylbenzenesulphonamide [8] as white needles, m. p. and mixed m. p. 180—181°.

The combined filtrate and washings (A) were acidified with 2N-sulphuric acid, and the solid was separated, washed free from sulphate, and dried, giving material (1·02 g.) of m. p. 139—143°. Recrystallisation from aqueous alcohol provided pure 2,4,6-trimethylbenzenesulphonamide,[8] m. p. and mixed m. p. 143—144°.

The authors thank Dr. G. Baddeley and Dr. P. C. Crofts for their interest and advice. Microanalyses were carried out by Mr. V. Manohin.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY,
MANCHESTER, 1. [*Received, June 5th,* 1961.]

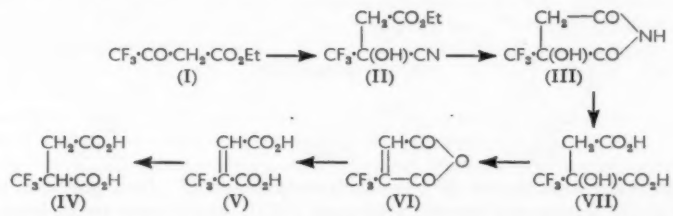
[13] Junghahn, *Ber.*, 1902, **35**, 3750.
[14] Wallingford and Krueger, *Org. Synth.*, Coll. Vol. II, p. 353.
[15] Horning and Stromberg, *J. Amer. Chem. Soc.*, 1952, **74**, 2680.
[16] Gattermann, *Ber.*, 1899, **32**, 1136; Haworth and Lapworth, *J.*, 1923, **123**, 2982.

890. *Cyanohydrins of Ethyl γγγ-Trifluoroacetoacetate and 5,5,5-Trifluoro-4-oxopentanoic Acid.*

By J. Burdon, T. J. Smith, and J. C. Tatlow.

The cyanohydrins of ethyl γγγ-trifluoroacetoacetate (I) and 5,5,5-trifluoro-4-oxopentanoic acid (VIII) have been prepared by the usual method. That from the former has been hydrolysed to α-hydroxy-α-trifluoromethylsuccinic acid (VII), which was converted into α-trifluoromethylsuccinic acid (IV) by way of α-trifluoromethylmaleic acid (V). The pentanoic cyanohydrin (IX) has been hydrolysed to the corresponding acid lactone (XIII).

Ethyl acetoacetate has been converted into the corresponding cyanohydrin by a number of methods,[1,2] including treatment with aqueous potassium cyanide.[2] In an analogous manner we have prepared ethyl β-cyano-γγγ-trifluoro-β-hydroxybutyrate (II) in 56% yield from ethyl γγγ-trifluoroacetoacetate (I) by treatment with aqueous potassium cyanide at 0°, followed by sulphuric acid. The main reactions we have carried out, starting from this cyanohydrin (II), are summarised in the reaction scheme.



Mild acidic hydrolysis of the cyanohydrin (II) gave α-hydroxy-α-trifluoromethylsuccinimide (III) and not the corresponding ester-amide which was, however, almost certainly an intermediate in the hydrolysis and not unexpectedly cyclised during the reaction. More drastic hydrolysis gave the hydroxy-acid (VII), which was dehydrated fairly readily with phosphoric oxide to α-trifluoromethylmaleic anhydride (VI). Hydrolysis of this anhydride with cold dilute sulphuric acid gave the maleic acid (V): treatment with boiling water for only a few minutes liberated a small amount of fluoride ion, and use of 2N-alkali led to a much more extensive hydrolysis of the trifluoromethyl group. This is in line with the observation by Buxton, Stacey, and Tatlow,[3] that α-trifluoromethylacrylic acid and its derivatives lost fluoride ion very easily, even on treatment with boiling water. The ultraviolet spectrum of the maleic acid (V) [$\lambda_{max.}$ 207 mμ, ε 11,500] was very similar to that of maleic acid itself [$\lambda_{max.}$ 209 mμ, ε 12,000 [4]]. That this acid (V) was the *cis*- and not the *trans*-isomer is indicated by the very mild conditions under which it was obtained from the anhydride (VI), and by its relative ease of cyclisation back into the anhydride: even at 140°, approximately 10% of the anhydride (VI) had been formed after 1 hr. Maleic acid and its homologues are known [5] to be dehydrated easily at 160° and below, whereas fumaric acids are stable up to 200° at least.

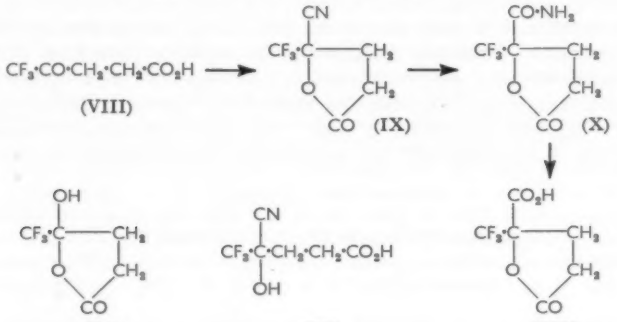
Attempts have been made to convert the maleic acid (V) into its fumaric isomer. Treatment with a small amount of bromine in chloroform [5] and with sulphuric acid were both ineffective. Owing to the size of the trifluoromethyl group it is, of course, possible that the maleic acid (V) is the favoured form and not the fumaric isomer, as is usually the case [5] with these types of compound.

[1] Demarçay, *Compt. rend.*, 1876, **82**, 1337; Mowry and Rossow, *J. Amer. Chem. Soc.*, 1945, **67**, 926.
[2] Bucherer and Grolee, *Ber.*, 1906, **39**, 1224.
[3] Buxton, Stacey, and Tatlow, *J.*, 1954, 366.
[4] Ley and Wingchen, *Ber.*, 1934, **67**, 501.
[5] Rodd, "Chemistry of Carbon Compounds." Elsevier, London, Vol. 1B, 1952, pp. 987—1002.

XUM

The maleic acid (V) could not be hydrogenated to α-trifluoromethylsuccinic acid (IV) over Raney nickel: fluoride ion was liberated, presumably owing to the residual alkali present in this catalyst when it is prepared in the usual way. The reduction has, however, been effected in 34% yield with hydriodic acid and red phosphorus. Like other β-fluoro-acids [3] possessing an α-hydrogen atom, the succinic acid (IV) lost fluoride ion readily with dilute alkali.

The γγγ-trifluoro-analogue [6] (VIII) of lævulic acid, on being treated with aqueous potassium cyanide and then sulphuric acid, also gave a cyanohydrin (IX) (59% yield). This compound and the amide (X) and acid (XIII) derived from it, exist as lactones, and not as free acids [cf. (XII)]. Lævulic acid cyanohydrin and the acid obtained from



it by hydrolysis are also known to have lactone structures.[7] In a previous paper [6] we suggested that the fluorinated lævulic acid itself (VIII) might exist in an isomeric cyclic form (XI). The infrared absorption of the cyanohydrin (IX) in the carbonyl region at 1830 cm.$^{-1}$ is also consistent [8] only with the lactone structure.

Experimental

Ethyl β-Cyano-γγγ-trifluoro-β-hydroxybutyrate (II).—A solution of potassium cyanide (15·0 g., 0·231 mole) in water (30 ml.) was added, with stirring, during 30 min. to an ice-cooled solution of ethyl γγγ-trifluoroacetoacetate (I) (30 g., 0·163 mole) in ethanol (100 ml.) and water (150 ml.). The mixture was stirred for 8 hr. at 0° and then acidified with 6N-sulphuric acid (125 ml.) and extracted continuously with ether for 18 hr. Distillation of the dried ($MgSO_4$) extracts afforded unchanged ethyl γγγ-trifluoroacetoacetate (4·5 g.), b. p. 28—36°/12 mm., identified by its infrared spectrum, and the crude product (16·4 g.), b. p. 92—96°/12 mm., which was redistilled to give *ethyl β-cyano-γγγ-trifluoro-β-hydroxybutyrate* (II) (12·3 g.), b. p. 93—94°/12 mm., n_D^{16} 1·3850 (Found: C, 40·0; H, 4·0. $C_7H_8F_3NO_3$ requires C, 39·8; H, 3·8%).

The crude product from the initial distillation was used for the later conversions.

When the reaction mixture was stirred at room temperature for 14 hr. it became very dark and only a 26% yield of the cyanohydrin was obtained.

4-Cyano-5,5,5-trifluoro-4-hydroxypentanoic Acid Lactone (IX).—5,5,5-Trifluoro-4-oxopentanoic acid [6] (VIII) (17·0 g., 0·10 mole) was neutralised with aqueous sodium hydrogen carbonate, and the solution was made up to 150 ml. This was cooled to 0° and potassium cyanide (6·5 g., 0·10 mole) in water (25 ml.), pre-cooled to 0°, was added, with stirring, during 30 min. The mixture was stirred at 0° for 7 hr. and then at room temperature for a further 16 hr. Acidification with 8N-sulphuric acid (25 ml.), followed by isolation as in the previous experiment, yielded *4-cyano-5,5,5-trifluoro-4-hydroxypentanoic acid lactone* (IX) (10·5 g.), b. p. 52·5—54·5°/0·3 mm., n_D^{16} 1·3916, $\nu_{max.}$ 1830 cm.$^{-1}$ (Found: C, 40·4; H, 2·5. $C_6H_4F_3NO_2$ requires C, 40·2; H, 2·3%).

[6] Brown, Burdon, Smith, and Tatlow, *Tetrahedron*, 1960, **10**, 164.
[7] Adams and Hauserman, *J. Amer. Chem. Soc.*, 1952, **74**, 694.
[8] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen & Co., London, 1954, pp. 159, 160.

Hydrolysis of the Cyanohydrins to the Amides.—(a) *α-Hydroxy-α-trifluoromethylsuccinimide* (III). Ethyl β-cyano-γγγ-trifluoro-β-hydroxybutyrate (II) (2·2 g.) and sulphuric acid (2 ml.; *d* 1·84) were heated together at 110—120° for 1 hr. The solution was cooled to 0°, water (50 ml.) was added, and the crude product was isolated by ether extraction. Recrystallisation from benzene gave *α-hydroxy-α-trifluoromethylsuccinimide* (III) (1·7 g.), m. p. 118—119° (Found: C, 32·7; H, 2·2. $C_5H_4F_3NO_3$ requires C, 32·8; H, 2·2%).

(b) *4-Carbamoyl-5,5,5-trifluoro-4-hydroxypentanoic acid lactone* (X). The cyanohydrin (IX) (2·2 g.) was treated with sulphuric acid (2 ml.; *d* 1·84) as in (a), to give the *amide* (X) (1·8 g.), m. p. 136—137° (from water), $\nu_{max.}$ 1637, 1718, and 1810 cm.$^{-1}$ (Found: C, 37·0; H, 3·3. $C_6H_6F_3NO_3$ requires C, 36·6; H, 3·1%).

Hydrolysis of the Amides to the Acids.—(a) *α-Hydroxy-α-trifluoromethylsuccinic acid* (VII). The imide (III) (4·15 g.) was refluxed with 6N-sulphuric acid (50 ml.) for 17 hr. Extraction with ether, followed by evaporation of the dried ($MgSO_4$) extracts, left a gum (4·5 g.), which was distilled [130—150° (bath)/15 mm.]. The distillate solidified in a vacuum-desiccator over phosphoric oxide to give the hygroscopic *acid* (VII), m. p. 122—124° (Found: C, 29·7; H, 2·7%; equiv., 102. $C_5H_5F_3O_5$ requires C, 29·7; H, 2·5%; equiv., 101).

A neutralised aqueous solution of the acid, on treatment with aqueous *S*-benzylthiouronium chloride, gave the *bis*-S-*benzylthiouronium salt*, m. p. 168° (decomp.) (from aqueous ethanol) (Found: C, 46·9; H, 5·0. $C_{21}H_{25}F_3N_4O_5S_2$ requires C, 47·2; H, 4·7%).

(b) *4-Carboxy-5,5,5-trifluoro-4-hydroxypentanoic acid lactone* (XIII). The amide (X) (0·30 g.) and 6N-sulphuric acid (10 ml.) were refluxed together for 8 hr. The crude product was isolated by continuous extraction with ether for 24 hr. and recrystallised from benzene, to give the *lactone* (XIII) (0·29 g.), m. p. 111—112° (Found: C, 36·7; H, 2·4%; equiv., 196. $C_6H_5F_3O_4$ requires C, 36·4; H, 2·5%; equiv., 198).

α-Trifluoromethylmaleic Anhydride (VI).—α-Hydroxy-α-trifluoromethylsuccinic acid (VII) (1·70 g.) was heated at 160—180° with an equal bulk of phosphoric oxide for 1 hr. The product was distilled *in vacuo* and then redistilled at atmospheric pressure, to give *α-trifluoromethylmaleic anhydride* (VI) (1·10 g.), b. p. 170—175° (Found: equiv., 85. $C_5HF_3O_3$ requires equiv., 83).

α-Trifluoromethylmaleic Acid (V).—A mixture of α-trifluoromethylmaleic anhydride (VI) (1·10 g.) and 4N-sulphuric acid (100 ml.) was left at room temperature until the anhydride had all dissolved (*ca.* 4 hr.). The solution was then extracted continuously with ether and the dried ($MgSO_4$) extracts were evaporated, to leave the slightly hygroscopic *α-trifluoromethylmaleic acid* (V) (1·12 g.), m. p. 99—104°, unchanged by recrystallisation from benzene, $\lambda_{max.}$ 207 mμ (ε 11,500 in water) (Found: C, 32·3; H, 2·0%; equiv., 95. $C_5H_3F_3O_4$ requires C, 32·6; H, 1·6%; equiv., 92).

Treatment of the acid with 2N-sodium hydroxide for 1 hr. at room temperature liberated fluoride ion. Infrared spectroscopy indicated that about 10% of the anhydride was formed when the acid was heated at 140° for 1 hr. The acid was recovered after being treated with concentrated sulphuric acid at room temperature for 3 days, or with boiling 2N-sulphuric acid for 3 hr., or with bromine (0·1 mol.) in chloroform in ultraviolet light for 8 hr.

The acid formed a *bis*-S-*benzylthiouronium salt*, m. p. 135—136° (decomp.) (from aqueous ethanol) (Found: C, 48·8; H, 4·5. $C_{21}H_{23}F_3N_4O_4S_2$ requires C, 48·8; H, 4·5%).

α-Trifluoromethylsuccinic Acid (IV).—α-Trifluoromethylmaleic acid (V) (0·81 g.), red phosphorus (*ca.* 0·4 g.), hydriodic acid (1·25 ml., *d* 1·70), and glacial acetic acid (12 ml.) were refluxed together for 3 hr., then diluted with water, acidified with sulphuric acid, filtered, and extracted continuously with ether. Evaporation of the dried ($MgSO_4$) extracts and recrystallisation of the residue from benzene gave *α-trifluoromethylsuccinic acid* (IV) (0·28 g.), m. p. 99°, depressed to 65—75° on admixture with the maleic acid (Found: C, 32·2; H, 2·9. $C_5H_5F_3O_4$ requires C, 32·3; H, 2·7%). Treatment of the acid with 2N-sodium hydroxide for 1 hr. at room temperature liberated fluoride ion.

The acid formed a *bis*-S-*benzylthiouronium salt*, m. p. 155—156° (from water) (Found: C, 48·5; H, 4·9. $C_{21}H_{25}F_3N_4O_4S_2$ requires C, 48·6; H, 4·9%).

We thank the Imperial Smelting Corporation for the award of a scholarship (to T. J. S.).

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, June 14th,* 1961.]

XUM

891. *Electric Dipole Moments of Substituted Pyridines, Pyridine 1-Oxides, and Nitrobenzenes.*

By A. N. Sharpe and S. Walker.

Twenty-seven dipole moments have been measured of alkyl, phenyl, and halogenated derivatives of the nitrobenzene, pyridine, and pyridine 1-oxide systems in benzene solution at 25° ± 0·01°. The dipole moments of the pyridine 1-oxides are very dependent on atmospheric humidity; consistent results can only be obtained when moisture is rigorously excluded. The electron-accepting power of the ring is compared for the three ring systems and for benzene. Correlations have been made from certain physical data for these molecules with Hammett substituent constants and mesomeric moments. The importance of hyperconjugation in determining the dipole moment in such systems is considered.

Chemical and dipole-moment evidence [1-3] has shown that the N–O group in pyridine 1-oxide is considerably stabilised by resonance with the ring. *X*-Ray-diffraction work [4] has shown that the N–O bond in 4-nitropyridine 1-oxide has about 25% double-bond character, and the C–C bonds parallel to the longitudinal axis of the molecule about 90% double-bond character. In this particular molecule, therefore, the quinonoid structure is relatively important. Further, dipole-moment studies [3] showed that the mesomeric moment of pyridine 1-oxide is larger for both electron-withdrawing and electron-releasing substituents than in the pyridine or benzene series.

The possible modes of interaction of the polar group with the ring in nitrobenzene, pyridine, and pyridine 1-oxide present interesting comparisons, and it was felt that a study of ring-substituent interaction in these systems would be informative. In addition, a study of the dipole moments of homologous series of the alkyl derivatives of these systems and of benzene offered a means of investigating hyperconjugation in the different types of conjugated molecules.

Experimental

Apparatus and Techniques.—The heterodyne-beat apparatus and the method of measurement have been previously described.[5] Seven solutions were generally made up; the dielectric constant and specific volume of pure benzene were assumed to be 2·2725 and 1·14445 respectively. Deviations between these values and the extrapolated values from the graphs never exceeded ±0·0005 and ±0·00002, respectively. Calculation of dipole moments has also been described and the results are considered to be accurate to within ±0·01 D, unless otherwise stated.

Solutions of deliquescent pyridine 1-oxides were prepared in a glove box. Reproducible results were obtained only when a vigorous stream of dry nitrogen was passed for at least 0·5 hr. before exposure of the compound. Pure benzene was added from a separatory funnel which had a ground-glass joint fitting the bottle neck, a sintered-glass filter plug, and a soda-lime tube to admit air. Solutions were transferred to and from the dielectric constant cell under pressure of dry air, and the temperature of the bath was controlled within ±0·01°.

Preparation and Purification of Materials.—The purification of benzene has been described previously.[5]

The following compounds were prepared by known methods and purified by crystallisation or fractionation in a column of high efficiency and low hold-up. Values of m. p. or b. p. from the literature are given in parentheses: pyridine 1-oxide (from benzene or ether), m. p. 66—67°

[1] Ochiai, summarizing paper, *J. Org. Chem.*, 1953, **18**, 534.
[2] Linton, *J. Amer. Chem. Soc.*, 1940, **62**, 1945.
[3] Katritzky, Randall, and Sutton, *J.*, 1957, 1769.
[4] Eichorn, *Acta Cryst.*, 1956, **9**, 787.
[5] Sharpe and Walker, *J.*, 1961, 2974.

(67° [6]); 4-methylpyridine 1-oxide (from benzene), m. p. 183° (185—186°,[7] 181° [8]), unchanged by further recrystallisation; 3-methylpyridine 1-oxide, m. p. 30°; 4-chloropyridine 1-oxide, (from acetone) m. p. 158° (decomp.), (from benzene), 149° (decomp.) (169·5°,[1] 152·5—153·5°,[9] 179·5—180° [10]); 4-bromopyridine 1-oxide (from acetone), m. p. 147° (decomp.), (from benzene), 142° (decomp.) [142—143°,[9] 163° (decomp.) [1]]; 3-chloropyridine 1-oxide b. p. 118—119°/1·05 mm., m. p. 54° (picrate, m. p. 141°); 3-bromopyridine 1-oxide, b. p. 124—126°/0·75 mm. (143—148°/4 mm.[11]), m. p. 43—44°; 3-iodopyridine 1-oxide (from benzene), m. p. 131° (picrate m. p. 145°); 4-bromopyridine,[12] distilled at −20° and evacuated at room temp.; 4-phenylpyridine 1-oxide [13] (from benzene), m. p. 151° (152—152·5° [13]); 3-chloropyridine, b. p.

TABLE 1.

10^6w_2	ε_{12}	v_{12}	n_{12}^2
Pyridine 1-oxide (dry nitrogen) *			
1209	2·2964	1·14398	2·24385
2069	2·3139	1·14368	2·24415
3639	2·3452	1·14313	2·24464
3648	2·3467	1·14312	2·24468
6607	2·4058	1·14203	2·24553
7442	2·4235	1·14172	2·24577
9841	2·4716	1·14084	2·24661

$\varepsilon_{12} = 2·2720 + 20·232w_2$;
$v_{12} = 1·14444 - 0·3651w_2$;
$n_{12}^2 = 2·24350 + 0·3144w_2$; ${}_2P_\infty = 383·95$ c.c.;
$R_D = 27·36$ c.c.; $\mu = 4·18$ D (ref. 2, 4·24).

* A second sample (see text) had the following values:
${}_2P_\infty = 387·63$ c.c.; $R_D = 27·81$ c.c.; $\mu = 4·20$ D. The dipole moment was taken to be 4·19 D (4·24[2]).

4-Propylpyridine 1-oxide *			
1053	2·2891	1·14422	2·24358
2513	2·3140	1·14388	2·24389
4338	2·3446	1·14346	2·24428
5201	2·3593	1·14323	2·24447
5230	2·3598	1·14324	2·24447
6275	2·3765	1·14298	2·24472
8305	2·4089	1·14252	2·24515

$\varepsilon_{12} = 2·2721 + 16·689w_2$;
$v_{12} = 1·14446 - 0·2336w_2$;
$n_{12}^2 = 2·24335 + 0·2170w_2$; ${}_2P_\infty = 467·80$ c.c.;
$R_D = 42·29$ c.c.; $\mu = 4·56$ D.

* A sample of this compound made into solutions in partially dried air had $\mu = 4·73$ D.

4-t-Butylpyridine 1-oxide.			
555	2·2809	1·14434	2·24354
1274	2·2929	1·14419	2·24373
2656	2·3143	1·14389	2·24410
2747	2·3157	1·14388	2·24413
3682	2·3302	1·14368	2·24436
4262	2·3397	1·14355	2·24451
7187	2·3835	1·14293	2·24528

$\varepsilon_{12} = 2·2725 + 15·637w_2$;
$v_{12} = 1·14446 - 0·2145w_2$;
$n_{12}^2 = 2·24340 + 0·2622w_2$; ${}_2P_\infty = 486·57$ c.c.;
$R_D = 48·76$ c.c.; $\mu = 4·63$ D.

4-Ethylpyridine 1-oxide.			
816	2·2878	1·14420	2·24360
1351	2·2974	1·14406	2·24376
1841	2·3066	1·14392	2·24391
2819	2·3237	1·14367	2·24422
2874	2·3258	1·14363	2·24422
3525	2·3380	1·14345	2·24444
4737	2·3604	1·14308	2·24480

$\varepsilon_{12} = 2·2725 + 18·477w_2$;
$v_{12} = 1·14444 - 0·2817w_2$;
$n_{12}^2 = 2·24334 + 0·3086w_2$; ${}_2P_\infty = 459·61$ c.c.;
$R_D = 38·47$ c.c.; $\mu = 4·54$ D.

4-Isopropylpyridine 1-oxide †			
503	2·2815	1·14436	2·24341
1502	2·2985	1·14409	2·24365
3051	2·3241	1·14375	2·24400
3119	2·3259	1·14371	2·24403
3398	2·3308	1·14363	2·24409
4572	2·3492	1·14336	2·24436
8083	2·4088	1·14255	2·24520

$\varepsilon_{12} = 2·2729 + 15·931w_2$;
$v_{12} = 1·14446 - 0·2407w_2$;
$n_{12}^2 = 2·24329 + 0·2360w_2$; ${}_2P_\infty = 473·75$ c.c.;
$R_D = 42·49$ c.c.; $\mu = 4·59$ D.

† A sample of this compound made into solutions in partially dried air had $\mu = 4·74$ D.

3-Methylpyridine 1-oxide *			
4110	2·3498	1·14323	2·24355
4863	2·3633	1·14304	2·24418
6716	2·4013	1·14244	2·24463
13,787	2·5346	1·14033	2·24533
21,071	2·6695	1·13822	2·24757
29,686	2·8363	1·13565	2·25024
50,824	3·2369	1·12945	2·25552

$\varepsilon_{12} = 2·2725 + 18·955w_2$;
$v_{12} = 1·14444 - 0·2954w_2$;
$n_{12}^2 = 2·24235 + 0·2638w_2$; ${}_2P_\infty = 416·65$ c.c.;
$R_D = 32·64$ c.c.; $\mu = 4·33$ D.

* The weight fractions are unusually high for this investigation as a result of the deceptive appearance of the solid (additions to bottles in the glove-box cannot be weighed). The concentrations are within the limits used by many authors, and the linearity was excellent.

[6] Rodd, "Chemistry of Carbon Compounds," Elsevier, Amsterdam, 1957, Vol. IVa.
[7] Boeckelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1286.
[8] Ochiai, *J. Pharm. Soc. Japan*, 1944, **64**, 72.
[9] den Hertog and Coombé, *Rec. Trav. chim.*, 1951, **70**, 581.
[10] Katritzky, *J.*, 1956, 2404.
[11] Murray and Hauser, *J. Org. Chem.*, 1954, **19**, 2008.
[12] Murray and Langham, *J. Amer. Chem. Soc.*, 1952, **74**, 6289.
[13] Katritzky and Hands, *J.*, 1958, 1754.

TABLE 1. (*Continued.*)

10^6w_2	ε_{12}	v_{12}	n_{12}^2
	4-*Phenylpyridine* 1-*oxide*		
888	2·2845	1·14414	2·24233
1690	2·2958	1·14385	2·24272
2501	2·3080	1·14352	2·24320
3552	2·3228	1·14312	2·24391
4443	2·3360	1·14279	2·24448
4646	2·3384	1·14269	2·24454
6943	2·3701	1·14187	2·24574

$\varepsilon_{12} = 2{\cdot}2723 + 14{\cdot}172w_2$;
$v_{12} = 1{\cdot}14447 - 0{\cdot}3775w_2$;
$n_{12}^2 = 2{\cdot}24178 + 0{\cdot}5863w_2$; ${}_2P_\infty = 492{\cdot}52$ c.c.;
$R_D = 57{\cdot}27$ c.c.; $\mu = 4{\cdot}61$ D.

	4-*Chloropyridine* 1-*oxide*		
1680	2·2844	1·14373	2·24290
2107	2·2875	1·14348	2·24314
3580	2·2975	1·14289	2·24352
3945	2·3003	1·14273	2·24382
5589	2·3116	1·14195	2·24415
5977	2·3149	1·14180	2·24433
6471	2·3178	1·14159	2·24463

$\varepsilon_{12} = 2{\cdot}2725 + 7{\cdot}034w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}4442w_2$;
$n_{12}^2 = 2{\cdot}24239 + 0{\cdot}3279w_2$; ${}_2P_\infty = 198{\cdot}42$ c.c.;
$R_D = 34{\cdot}68$ c.c.; $\mu = 2{\cdot}83$ D (ref. 3, 2·82).

	3-*Chloropyridine* 1-*oxide*		
2141	2·2976	1·14350	2·24397
2932	2·3073	1·14311	2·24424
4853	2·3295	1·14228	2·24502
4938	2·3309	1·14221	2·24505
7003	2·3545	1·14131	2·24577
8262	2·3688	1·14073	2·24619
10,575	2·3957	1·13971	2·24691

$\varepsilon_{12} = 2{\cdot}2726 + 11{\cdot}697w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}4496w_2$;
$n_{12}^2 = 2{\cdot}24325 + 0{\cdot}3538w_2$; ${}_2P_\infty = 311{\cdot}81$ c.c.;
$R_D = 35{\cdot}12$ c.c.; $\mu = 3{\cdot}68$ D.

	3-*Iodopyridine* 1-*oxide*		
1725	2·2854	1·14321	2·24337
1938	2·2868	1·14310	2·24334
2039	2·2872	1·14307	2·24334
5789	2·3159	1·14034	2·24460
7373	2·3267	1·13930	2·24475
8859	2·3373	1·13829	2·24523
15,259	2·3856	1·13376	2·24718

$\varepsilon_{12} = 2{\cdot}2725 + 7{\cdot}385w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}6998w_2$;
$n_{12}^2 = 2{\cdot}24276 + 0{\cdot}2906w_2$; ${}_2P_\infty = 336{\cdot}21$ c.c.;
$R_D = 41{\cdot}04$ c.c.; $\mu = 3{\cdot}79$ D.

	3-*Ethylpyridine*		
1695	2·2831	1·14431	2·24260
4192	2·2976	1·14413	2·24254
5523	2·3052	1·14403	2·24257
8399	2·3218	1·14381	2·24257
9075	2·3259	1·14377	2·24260
12,686	2·3468	1·14349	2·24257
14,234	2·3565	1·14337	2·24251

$\varepsilon_{12} = 2{\cdot}2730 + 5{\cdot}840w_2$;
$v_{12} = 1{\cdot}14444 - 0{\cdot}0747w_2$;
$n_{12}^2 = 2{\cdot}24258 - 0{\cdot}002w_2$; ${}_2P_\infty = 151{\cdot}81$ c.c.;
$R_D = 33{\cdot}54$ c.c.; $\mu = 2{\cdot}41$ D.

	4-*Methylpyridine* 1-*oxide*		
785	2·2882	1·14417	2·24421
1479	2·3033	1·14394	2·24445
1823	2·3101	1·14381	2·24451
2727	2·3292	1·14357	2·24495
2875	2·3317	1·14352	2·24505
3242	2·3388	1·14340	2·24517
4491	2·3644	1·14303	2·24565

$\varepsilon_{12} = 2{\cdot}2725 + 20{\cdot}560w_2$;
$v_{12} = 1{\cdot}14442 - 0{\cdot}3163w_2$;
$n_{12}^2 = 2{\cdot}24384 + 0{\cdot}4052w_2$; ${}_2P_\infty = 448{\cdot}90$ c.c.;
$R_D = 34{\cdot}92$ c.c.; $\mu = 4{\cdot}50$ D (ref. 3, 4·74).

	4-*Bromopyridine* 1-*oxide*		
1078	2·2786	1·14377	2·24270
1644	2·2815	1·14344	2·24290
2709	2·2878	1·14281	2·24313
3158	2·2897	1·14255	2·24327
3567	2·2919	1·14224	2·24335
6006	2·3053	1·14080	2·24403
6455	2·3086	1·14045	2·24412

$\varepsilon_{12} = 2{\cdot}2726 + 5{\cdot}492w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}6130w_2$;
$n_{12}^2 = 2{\cdot}24243 + 0{\cdot}2640w_2$; ${}_2P_\infty = 207{\cdot}29$ c.c.;
$R_D = 35{\cdot}85$ c.c.; $\mu = 2{\cdot}90$ D.

	3-*Bromopyridine* 1-*oxide*		
1540	2·2854	1·14352	2·24370
2143	2·2917	1·14317	2·24373
3029	2·2990	1·14263	2·24412
3959	2·3066	1·14205	2·24430
5976	2·3251	1·14086	2·24493
7535	2·3379	1·13986	2·24532
9197	2·3537	1·13881	2·24574

$\varepsilon_{12} = 2{\cdot}2724 + 8{\cdot}776w_2$;
$v_{12} = 1{\cdot}14446 - 0{\cdot}6088w_2$;
$n_{12}^2 = 2{\cdot}24323 + 0{\cdot}2765w_2$; ${}_2P_\infty = 314{\cdot}65$ c.c.;
$R_D = 36{\cdot}49$ c.c.; $\mu = 3{\cdot}69$ D.

	3-*Methylpyridine*		
2181	2·2872	1·14426	2·24276
3424	2·2956	1·14413	2·24274
5835	2·3116	1·14387	2·24274
6438	2·3163	1·14385	2·24280
7108	2·3208	1·14377	2·24276
11,181	2·3483	1·14335	2·24281
12,455	2·3571	1·14320	2·24284

$\varepsilon_{12} = 2{\cdot}2725 + 6{\cdot}775w_2$;
$v_{12} = 1{\cdot}14447 - 0{\cdot}1000w_2$;
$n_{12}^2 = 2{\cdot}24271 + 0{\cdot}008w_2$; ${}_2P_\infty = 147{\cdot}63$ c.c.;
$R_D = 28{\cdot}50$ c.c.; $\mu = 2{\cdot}41$ D.*

* Lit., (*a*) 2·40, (*b*) 2·30 D. (For refs. see p. 4526.)

	3-*Isopropylpyridine*		
1429	2·2796	1·14437	2·24247
2963	2·2880	1·14428	2·24242
4509	2·2957	1·14417	2·24233
6002	2·3034	1·14408	2·24230
7218	2·3101	1·14399	2·24224
8723	2·3183	1·14390	2·24221
12,408	2·3372	1·14366	2·24207

$\varepsilon_{12} = 2{\cdot}2723 + 5{\cdot}230w_2$;
$v_{12} = 1{\cdot}14446 - 0{\cdot}0638w_2$;
$n_{12}^2 = 2{\cdot}24253 - 0{\cdot}039w_2$; ${}_2P_\infty = 158{\cdot}20$ c.c.;
$R_D = 37{\cdot}45$ c.c.; $\mu = 2{\cdot}43$ D.

XUM

TABLE 1. (*Continued*).

10^6w_2	ε_{12}	v_{12}	n_{12}^2
	4-Phenylpyridine		
1008	2·2772	1·14427	2·24227
1617	2·2806	1·14412	2·24240
3216	2·2881	1·14369	2·24278
4682	2·2948	1·14339	2·24326
5353	2·2984	1·14317	2·24349
7781	2·3097	1·14260	2·24427
8688	2·3147	1·14238	2·24433

$\varepsilon_{12} = 2{\cdot}2725 + 4{\cdot}823w_2$;
$v_{12} = 1{\cdot}14446 - 0{\cdot}2350w_2$;
$n_{12}^2 = 2{\cdot}24192 + 0{\cdot}2745w_2$; $_2P_\infty = 182{\cdot}81$ c.c.;
$R_D = 50{\cdot}16$ c.c.; $\mu = 2{\cdot}55$ D.

	3-Chloropyridine		
1824	2·2800	1·14387	2·24340
3626	2·2871	1·14331	2·24344
4785	2·2919	1·14296	2·24346
7411	2·3022	1·14213	2·24372
8377	2·3059	1·14183	2·24378
9516	2·3015	1·14145	2·24388
14,660	2·3308	1·13984	2·24416

$\varepsilon_{12} = 2{\cdot}2726 + 3{\cdot}988w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}3139w_2$;
$n_{12}^2 = 2{\cdot}24320 + 0{\cdot}0685w_2$; $_2P_\infty = 113{\cdot}26$ c.c.;
$R_D = 29{\cdot}12$ c.c.; $\mu = 2{\cdot}02$ D.*

* Lit.,[d] 2·02 D (for ref. see p. 4526).

	3-Iodopyridine		
719	2·2740	1·14397	2·24188
2332	2·2773	1·14299	2·24221
2535	2·2779	1·14284	2·24224
3802	2·2805	1·14199	2·24245
4046	2·2812	1·14192	2·24245
4556	2·2824	1·14158	2·24257
7633	2·2888	1·13964	2·24316

$\varepsilon_{12} = 2{\cdot}2724 + 2{\cdot}154w_2$;
$v_{12} = 1{\cdot}14442 - 0{\cdot}6249w_2$;
$n_{12}^2 = 2{\cdot}24174 + 0{\cdot}187w_2$; $_2P_\infty = 114{\cdot}79$ c.c.;
$R_D = 38{\cdot}50$ c.c.; $\mu = 1{\cdot}93$ D.

	m-*Chloronitrobenzene*		
1034	2·2811	1·14405	2·24356
1894	2·2885	1·14368	2·24380
3514	2·3009	1·14299	2·24397
4621	2·3106	1·14251	2·24406
5961	2·3220	1·14197	2·24436
7490	2·3342	1·14132	2·24454
7839	2·3376	1·14118	2·24463

$\varepsilon_{12} = 2{\cdot}2725 + 8{\cdot}265w_2$;
$v_{12} = 1{\cdot}14447 - 0{\cdot}4201w_2$;
$n_{12}^2 = 2{\cdot}24347 + 0{\cdot}143w_2$; $_2P_\infty = 278{\cdot}93$ c.c.;
$R_D = 37{\cdot}74$ c.c.; $\mu = 3{\cdot}44$ D.*

* Lit.,[b] 3·38, 3·18, 3·12, 3·40 D.

10^6w_2	ε_{12}	v_{12}	n_{12}^2
	4-Bromopyridine *		
1427	2·2734	1·14371	2·24308
3196	2·2747	1·14272	2·24343
3465	2·2750	1·14250	2·24349
4361	2·2755	1·14213	2·24358
7500	2·2773	1·14040	2·24400
11,220	2·2801	1·13850	2·24454
19,088	2·2849	1·13436	2·24565

$\varepsilon_{12} = 2{\cdot}2726 + 0{\cdot}6507w_2$;
$v_{12} = 1{\cdot}14444 - 0{\cdot}5325w_2$;
$n_{12}^2 = 2{\cdot}24295 + 0{\cdot}1414w_2$; $_2P_\infty = 48{\cdot}14$ c.c.;
$R_D = 32{\cdot}59$ c.c.; $\mu = 0{\cdot}77 \pm 0{\cdot}02$ D (0·79).†

* An allowance of 4·9 c.c. was made by Katritzky, Randall, and Sutton [3] for the P_A of 4-chloropyridine, being the sum of the P_A terms for chlorobenzene (3·9 c.c.) and pyridine (1·5 c.c.) less the P_A term for benzene (0·55 c.c.). A similar allowance of 3·5 c.c. was made for the P_A of 4-bromopyridine, from the P_A of bromobenzene (2·5 c.c.) (ref. *c*, p. 4526).

† Cumper and Vogel's figure [d] recalculated by taking $P_A = 3{\cdot}5$ c.c.

	3-Bromopyridine		
945	2·2751	1·14396	2·24287
1880	2·2775	1·14343	2·24302
3901	2·2833	1·14240	2·24311
5571	2·2881	1·14150	2·24337
6446	2·2907	1·14104	2·24358
8492	2·2964	1·13996	2·24364
11,243	2·3044	1·13848	2·24400

$\varepsilon_{12} = 2{\cdot}2722 + 2{\cdot}861w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}5997w_2$;
$n_{12}^2 = 2{\cdot}24275 + 0{\cdot}113w_2$; $_2P_\infty = 113{\cdot}97$ c.c.;
$R_D = 31{\cdot}86$ c.c.; $\mu = 2{\cdot}00$ D.*

* Lit., (*d*) 2·02, (*e*) 1·93 D (for refs. see p. 4526).

	p-*Chloronitrobenzene*		
732	2·2759	1·14415	2·24304
2095	2·2822	1·14360	2·24319
3683	2·2908	1·14288	2·24334
4509	2·2937	1·14255	2·24349
5886	2·3009	1·14198	2·24367
5897	2·3011	1·14197	2·24367
10,459	2·3227	1·14007	2·24418

$\varepsilon_{12} = 2{\cdot}2724 + 4{\cdot}825w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}4194w_2$;
$n_{12}^2 = 2{\cdot}24293 + 0{\cdot}122w_2$; $_2P_\infty = 177{\cdot}02$ c.c.;
$R_D = 37{\cdot}15$ c.c.; $\mu = 2{\cdot}62$.*

* Lit.,[b] 2·52, 2·55, 2·36, 2·34, 2·57, 3·12 D (for ref. see p. 4526).

	p-*Bromonitrobenzene*		
903	2·2760	1·14395	2·24328
2332	2·2816	1·14312	2·24354
3033	2·2846	1·14266	2·24370
3776	2·2875	1·14222	2·24382
4997	2·2921	1·14157	2·24421
7166	2·3010	1·14035	2·24466
7923	2·3039	1·13985	2·24478

$\varepsilon_{12} = 2{\cdot}2722 + 4{\cdot}026w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}5785w_2$;
$n_{12}^2 = 2{\cdot}24306 + 0{\cdot}218w_2$; $_2P_\infty = 187{\cdot}02$ c.c.;
$R_D = 41{\cdot}90$ c.c.; $\mu = 2{\cdot}66$ D.*

* Lit.,[b] 2·69, 2·53, 2·45, 2·65 D (for ref. see p. 4526).

TABLE 1. (*Continued.*)

10^6w_2	ε_{12}	v_{12}	n_{12}^2
	m-*Bromonitrobenzene*		
2048	2·2855	1·14332	2·24305
3104	2·2924	1·14270	2·24326
4345	2·3005	1·14200	2·24348
5861	2·3108	1·14112	2·24364
7445	2·3207	1·14026	2·24393
7552	2·3216	1·14009	2·24393
9422	2·3332	1·13906	2·24421

$\varepsilon_{12} = 2{\cdot}2722 + 6{\cdot}519w_2$;
$v_{12} = 1{\cdot}14448 - 0{\cdot}5735w_2$;
$n_{12}^2 = 2{\cdot}24271 + 0{\cdot}164w_2$; ${}_2P_\infty = 282{\cdot}05$ c.c.;
$R_D = 40{\cdot}12$ c.c.; $\mu = 3{\cdot}44$ D.*

† Lit.,[b] 3·17, 3·41 (for ref. see p. below).

10^6w_2	ε_{12}	v_{12}	n_{12}^2
	m-*Iodonitrobenzene*		
650	2·2759	1·14401	2·24337
2202	2·2846	1·14301	2·24364
3199	2·2900	1·14235	2·24385
3963	2·2945	1·14185	2·24400
9462	2·3254	1·13824	2·24493
10,635	2·3320	1·13743	2·24511
11,314	2·3358	1·13706	2·24524

$\varepsilon_{12} = 2{\cdot}2722 + 5{\cdot}619w_2$;
$v_{12} = 1{\cdot}14445 - 0{\cdot}6579w_2$;
$n_{12}^2 = 2{\cdot}24328 + 0{\cdot}173w_2$; ${}_2P_\infty = 299{\cdot}27$ c.c.;
$R_D = 43{\cdot}73$ c.c.; $\mu = 3{\cdot}54$ D.*

* Lit.,[b] 3·22, 3·62 D (for ref. see below).

10^6w_2	ε_{12}	v_{12}	n_{12}^2
	p-*Iodonitrobenzene*		
1687	2·2793	1·14340	2·24225
2332	2·2815	1·14292	2·24253
3761	2·2872	1·14202	2·24281
5219	2·2929	1·14106	2·24323
6286	2·2968	1·14036	2·24343
7705	2·3025	1·13935	2·24373
8470	2·3055	1·13890	2·24397

$\varepsilon_{12} = 2{\cdot}2725 + 3{\cdot}897w_2$;
$v_{12} = 1{\cdot}14446 - 0{\cdot}6546w_2$;
$n_{12}^2 = 2{\cdot}24190 + 0{\cdot}244w_2$; ${}_2P_\infty = 218{\cdot}87$ c.c.;
$R_D = 47{\cdot}33$ c.c.; $\mu = 2{\cdot}90$ D.*

† Lit.,[b] 3·04, 2·63 D (for ref. see below).

Refs.: (*a*) Cumper, Vogel, and Walker, *J.*, 1956, 3621. (*b*) Wesson, " Tables of Electric Dipole Moments," Technology Press, Cambridge, Mass. (*c*) Huang and Sullivan, *Nature*, 1960, **188**, 1104. (*d*) Cumper and Vogel, *J.*, 1960, 4723. (*e*) Goethals, *Rec. Trav. chim.*, 1935, **54**, 299.

147·5°/754 mm. (148°/744 mm.[14]); 3-bromopyridine,[15] b. p. 171°/751 mm. (169—170° [14], 173° [14], 173·7—174°/762 mm.[15]); 3-iodopyridine,[16] m. p. 53—54° (52° [16], 53·5° [14]); 3-isopropylpyridine,[17] b. p. 179°/750 mm. (179·3° [17]) [picrate, m. p. 138·5° (138·1—138·6° [17])].

The halogenonitrobenzenes were commercial samples or prepared by diazotisation. All were steam-distilled and fractionally crystallised from light petroleum: *m*-chloro-, m. p. 45·5° (46° [14]), *m*-bromo-, m. p. 56·5° (56° [14]), *m*-iodo-, m. p. 38° (38·5° [14]), *p*-chloro-, m. p. 83° (83° [14]), *p*-bromo-, m. p. 127° (127° [14]), and *p*-iodo-nitrobenzene, m. p. 174·5° (174° [14]).

Solid samples were stored under a high vacuum in the presence of phosphoric oxide and wax shavings in the dark for at least 2 days before use. For deliquescent compounds the desiccator was refilled with dry nitrogen. Liquids were used immediately after distillation, or, where this was impossible, were stored in the dark in small Quickfit stoppered flasks with a minimum of air space.

DISCUSSION

The two results for pyridine 1-oxide, which are for different samples, one crystallised from benzene and weighed out in an atmosphere of nitrogen, and the other crystallised from ether and weighed out in an atmosphere of carefully dried air, are identical within the limits of experimental error, but differ significantly from the value obtained by Linton,[2] who stated that drying trains were used but did not stress the importance of exclusion of moisture. The difference (0·23 D) between the value for 4-methylpyridine 1-oxide and that obtained by Katritzky, Randall, and Sutton [3] is probably due to the effect of water; no mention of special precautions was made in their paper; the value obtained for 4-chloropyridine 1-oxide, which is not particularly hygroscopic, is identical within the limits of

[14] Heilbron, " Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1936.
[15] den Hertog and Wibaut, *Rec. Trav. chim.*, 1932, **51**, 949.
[16] Gergely and Iredale, *J.*, 1953, 3232.
[17] Brown and Murphey, *J. Amer. Chem. Soc.*, 1951, **73**, 3308.

experimental error with the value obtained by these workers. The water probably exerts its effect by forming a highly polar hydroxide. No changes were observed under differing conditions with the substituted pyridines and nitrobenzenes.

TABLE 2.

Comparison of moments calculated with and without inclusion of the inductive effect.

Subst.	$\mu_{obs.}$	$\mu_{calc.}$*	$\mu_{corr.}$†	Subst.	$\mu_{obs.}$	$\mu_{calc.}$*	$\mu_{corr.}$†
			Nitrobenzene				
3-Me	4·14	4·21	4·28	4-Me	4·42	4·38	4·44
3-Cl	3·44	3·50	3·50	4-Bu^t	4·61	4·46	4·58
3-Br	3·44	3·50	3·51	4-Cl	2·62	2·43	2·46
3-I	3·54	3·52	3·57	4-Br	2·66	2·45	2·51
				4-Ph	4·36	4·01	4·18
			Pyridine				
3-Me	2·41	2·42	2·46	4-Me	2·60	2·59	2·63
3-Cl	2·02	1·98	1·96	4-Bu^t	2·73	2·66	2·75
3-Br	2·00	1·98	1·96	4-Cl	0·78	0·64	0·67
3-I	1·93	1·94	1·92	4-Br	0·77	0·66	0·70
				4-Ph	2·55	2·21	2·32
			Pyridine 1-oxide				
3-Me	4·33	4·37	4·45	4-Me	4·50	4·55	4·63
3-Cl	3·69	3·66	3·66	4-Bu^t	4·63	4·64	4·80
3-Br	3·69	3·65	3·67	4-Cl	2·83	2·60	2·65
3-I	3·79	3·68	3·71	4-Br	2·90	2·62	2·69
				4-Ph	4·62	4·19	4·38

* Calc. without inclusion of the inductive effect.
† Calc. with inclusion of the inductive effect.

The bond lengths and angles in pyridine (and presumably pyridine 1-oxide) differ from those in benzene.[18] This difference is certain to mean differing electronegativities of the ring-carbon atoms in the two systems, and this in turn will affect both the C–X moment and the unsubstituted C–H moments. It would, thus, be unwise to expect the calculated moment, even for a substituent with a low mesomeric and induced moment, to be identical with the observed moment.

In Table 2 values obtained by summation of the moments of the parent compounds and the corresponding substituted benzenes ($\mu_{calc.}$) are compared with values obtained by allowing for the classical inductive effect ($\mu_{corr.}$) in a way similar to that used by Smith and Littlejohn for monosubstituted biphenyls.[19]

The dipole moment induced in a substituent by a dipole μ may be estimated from the equations:[20]

$$\mu_x = \frac{\mu\gamma(\varepsilon_b + 2)}{3\varepsilon_a r^3} \ (3\cos^2\theta - 1)$$

$$\mu_y = \frac{\mu\gamma(\varepsilon_b + 2)}{\varepsilon_a r^3} \cdot \sin\theta\cos\theta$$

where μ_x and μ_y are the moments induced along the x and the y axis, respectively, in the plane containing the polarisable centre and the polarising dipole, the line from the polarisable centre to the dipole being inclined at an angle θ to the axis of the dipole: ε_a is the dielectric constant of the material between the dipole and the polarisable centre, and ε_b the dielectric constant of the polarisable material. Both ε_a and ε_b were taken as 2·3, the dielectric constant of benzene, and the polarisabilities γ were calculated from the appropriate bond refractions.[21] In the case of pyridine, the polarising dipole was

[18] Bak, Hansen, and Rastrup-Anderson, *J. Chem. Phys.*, 1954, **22**, 2013.
[19] Smith and Littlejohn, *J.*, 1953, 2456; 1954, 2552.
[20] Smith, "Electric Dipole Moments," Butterworths, London, 1955.
[21] Smallwood and Herzfeld, *J. Amer. Chem. Soc.*, 1930, **52**, 1919.

XUM

assumed to be situated in the region of the nitrogen atom and to be about 1·8 D.[22] Three sets of values, corresponding to a polarising dipole located up to 0·2 Å from the nitrogen atom did not differ by more than 0·01 D.

Except for alkyl compounds, the moments calculated with inclusion of the inductive effect are generally closer to the observed values than those without, although the agreement is still not good. The calculated moments of the alkyl compounds are, in general, larger than the observed moments, the remainder generally smaller.

Chemical and previous dipole-moment evidence indicates that the mesomeric effect of substituents attached to the pyridine ring is higher for electron-releasing and lower for electron-withdrawing substituents than in the benzene series, and that it is greater for both types of substituent in the 4-position of pyridine 1-oxide than in the pyridine or benzene series. This conclusion is supported by infrared work.[23] The results in the present work, which are only for electron-releasing substituents, or substituents whose mesomeric moment is directed towards the ring, agree with such conclusions. In addition, the interaction moments in Table 3, which reflect changes in induced and mesomeric moments relative to the corresponding groups in benzene, indicate that the electron-accepting power of the nitrobenzene ring lies between those of pyridine and pyridine 1-oxide.

Estimates have been made of the C–H bond moment in pyridine and benzene [24] but cannot yet be made for pyridine 1-oxide, and the $\mu_{int.}$ values are dependent on the C–H bond moment differences in these systems. This is borne out by the relative order of the

TABLE 3.

Interaction moments [a] (D) ($\mu_{int.} = \mu_{obs.} - \mu_{calc.}$).

4-Subst.	Benzene	Pyridine	Nitrobenzene	Pyridine 1-oxide
NO_2	0	+0·22 [b]	—	+0·51 [b, e]
CN	0	+0·17 [b]	—	—
Cl	0	+0·15 [b]	+0·19 [c]	+0·22 [c]
Br	0	+0·12 [c]	+0·21 [c]	+0·27 [c]
Me	0	+0·02 [d]	+0·04 [a]	−0·06 [c]
Bu^t	0	+0·07 [d]	+0·15 [f]	+0·01 [c]
Ph	0	+0·34 [a]	+0·35 [a]	+0·42 [c]
MeO	0	+0·14 [b]	+0·32 [a]	+0·40 [b]
NMe_2	0	+0·95 [b]	+1·48 [a]	+1·52 [b]

[a] Bond angles and moments used in obtaining $\mu_{int.}$ were taken from Smith (ref. 20, p. 209). [b, d, f] Observed values from refs. 3, 24, and 23, respectively. [c] This investigation. [e] $\mu_{obs.}$ taken as 0·69 D; [3] this is probably too high through neglect of P_A, and the workers suggest that the actual moment is indistinguishable from zero.

interaction moments for the alkyl substituents, which for these dipoles of small magnitude suggests that the values are governed by C–H bond-moment variations. The values of $\mu_{CX} - \mu_{OH}$ (see Table 4) indicate a similar order of electron-accepting power. When the calculated induced moments are allowed for, the order is unchanged.

Since Hammett substituent constants are a measure of the interaction between a substituent and the ring, linear relations are frequently found between the σ values and sets of physical data.[25,26] A linear relation between dipole moments and σ value for *para*- and apparently also *meta*-substituted nitrobenzenes, chlorobenzenes, and anilines has been reported.[26] A linear plot is obtained for dipole moment of 4-substituted pyridines and pyridine 1-oxides against σ-value; this is not the case for 3-substituents,

[22] Cumper, *Chem. and Ind.*, 1958, 1628.
[23] Katritzky, *Quart. Rev.*, 1959, **13**, 353.
[24] Cumper, Vogel, and Walker, *J.*, 1956, 3621.
[25] Rao, *Chem. and Ind.*, 1956, 666; Whetsel, Roberson, and Krell, *Analyt. Chem.*, 1958, **30**, 1598; Rao, Wahl, and Williams, *Canad. J. Chem.*, 1957, **35**, 1575.
[26] van Beek, *Rec. Trav. chim.*, 1957, **76**, 729.

TABLE 4.

Calculated differences in moments (D), C–X minus C–H.

3-Subst.	Benzene	Pyridine [a]	Nitrobenzene [b]	Pyridine 1-oxide [d]
Me	+0·37	+0·35	+0·37	+0·27
Cl	−1·58	−1·73	−(1·71, 1·53)	−1·43
Br	−1·56	−1·64	−(1·71, 1·53) [c]	−1·43
I	−1·40	−1·35	−(1·16, 1·02) [c]	−1·00
4-Subst.				
Me	+0·37	+0·39	+0·41	+0·31
Bu^t	+0·45	+0·52	+0·60	+0·44
Cl	−1·58	−1·43	−1·39	−1·36
Br	−1·56	−1·44	−1·35	−1·29
I	−1·40	—	−1·11	—
Ph	0	+0·34	+0·35	+0·42

[a] Calc. by assuming μ(pyridine) = 2·21 D.[21] [b] Calculated for 4-substituted compounds by assuming $\mu(NO_2)$ = 4·01 D.[20] [c] Using 4·01 D for $\mu(NO_2)$ gives complex values for halogen substituents. Values shown were arrived at by assuming μ(CMe) = 0·37 D (Cumper, Vogel, and Walker, *J.*, 1957, 3640) in 3-nitrotoluene (μ = 4·14 or 4·17 D) (ref. *b*, p. 4526), giving $\mu(NO_2)$ = 3·94 and 3·96 D, respectively. This illustrates the large possible error for 3-substituted compounds. [d] Calc. by assuming μ(pyridine oxide) = 4·19 D.

where the actual dipole moment acts at an angle to the direction of the electronic displacements, depending on the relative magnitudes of the substituent moments, and may not

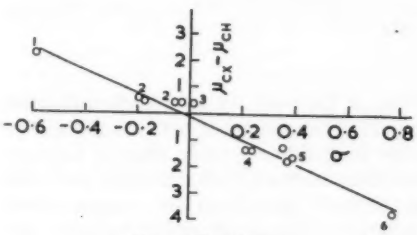


Fig. 1, Pyridines.

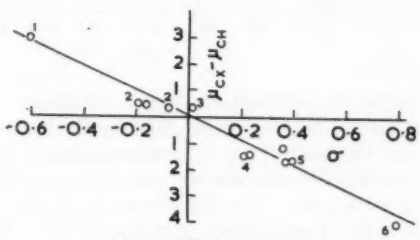


Fig. 2, Nitrobenzenes.

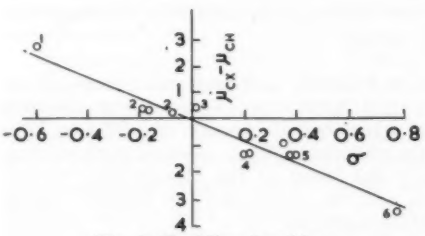


Fig. 3, Pyridine 1-oxides.

FIGS. 1—3. Differences in calculated moments, C–X minus C–H, plotted against σ-values.

1, 4-NMe_2. 2, 3- and 4-Alkyl. 3, 4-Ph. 4, 4-Hal. 5, 3-Hal. 6, 4-NO_2.

reflect in a simple manner the degree of interaction between the groups. If C–X *minus* C–H moments of both 3- and 4-substituents are plotted against σ values [27] (see Figs. 1, 2, and 3) a good approach to linearity is obtained.

Plots of extinction coefficient and stretching frequency [28] against σ value for the N–O group in substituted pyridine 1-oxides show good linearity, and deviations by the methylamino-, dimethylamino-, cyano-, and nitro-groups indicate electron drift towards the ring relative to that in benzene.

The integrated absorption intensity of the N–O in-plane bending vibration should

[27] Jaffé, *Chem. Rev.*, 1953, **53**, 191.
[28] Katritzky and Gardner, *J.*, 1958, 2192.

XUM

be a function of the dipole moment of the group and hence of the mesomeric moment of this group with the remainder of the molecule. Katritzky [23] suggests that the bands occurring at about 850 cm.$^{-1}$ may be due to this vibrational mode. A plot of the maximum extinction coefficients of these bands against mesomeric moment (as calculated by Katritzky, Randall, and Sutton [3]) is shown in Fig. 4. It is surprising that, as the electron-releasing power of the substituent group is diminished, the extinction coefficient is increased.

On numerous occasions dipole moments have been used to indicate the importance of hyperconjugation in molecules.[29] One current view is that hyperconjugation is unimportant,[30] except perhaps in electronically excited or ionic species. Electron affinity increases significantly in the series, benzene < pyridine < nitrobenzene < pyridine 1-oxide, and important contributions from hyperconjugation in the alkyl derivatives might show up in marked differences in the moments of the methyl and the t-butyl group

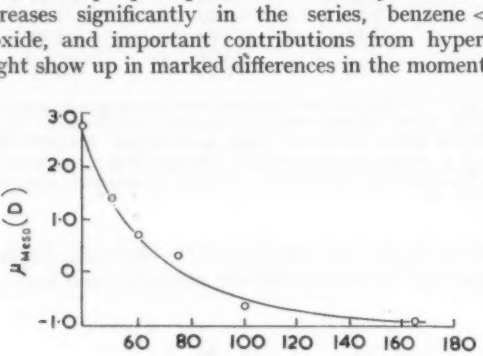


FIG. 4. Plot of mesomeric moment against extinction coefficient for the 850 cm.$^{-1}$ bands of pyridine 1-oxides. The points in order of decreasing μ_{Meso} values for the four substituents are NMe_2, OMe, Me, COMe, and NO_2.

under the different electronic conditions. Further, if the capacity for hyperconjugation is greater for the methyl than for the t-butyl group, then the difference between the methyl and the t-butyl group moments should be smaller in pyridine 1-oxide than in benzene. The dipole moments are considered to be reliable since a homologous series was measured in each case. The differences (corrected for electrostatic induction) are: benzene 0·08, pyridine 1-oxide 0·05, pyridine 0·08 D. The similarity of these differences suggests that hyperconjugation is not important in determining the overall dipole moment of a molecule. An alternative but less likely explanation would be that hyperconjugation is of comparable importance for both the methyl and the t-butyl group.

One of us (A. N. S.) thanks the Department of Scientific and Industrial Research for a maintenance grant. We are also indebted to Dr. A. J. Nunn of this College for the synthesis of some of the substituted pyridine 1-oxides and a considerable amount of advice on their preparation, and to Mr. Palmer and Mr. Travers for preliminary dipole-moment work on these compounds. We also thank Mr. L. P. Priestley, the Head of the Department, for his interest, Mr. A. Clarke for technical assistance, and the University of London Central Research Fund for the loan of a standard variable air condenser.

SCHOOL OF CHEMISTRY, COLLEGE OF TECHNOLOGY,
LEICESTER.

[*Received, February 10th*, 1961.]

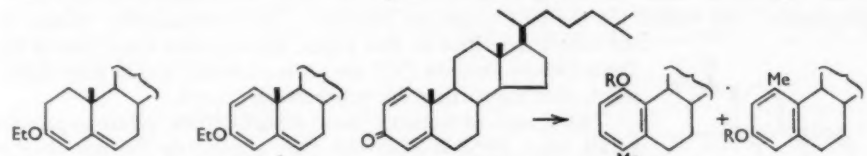
[29] See under " Hyperconjugation " in ref. 20.
[30] Dewar and Schmeising, *Tetrahedron*, 1959, **5**, 166; Brown, *J. Amer. Chem. Soc.*, 1959, **81**, 3232.

892. *Compounds Related to the Steroid Hormones. Part III.*[1] *Phenolic Ethers from the Dienone–Phenol Rearrangement of* $\Delta^{1,4}$*-3-Oxo-Steroids.*

By J. Elks, J. F. Oughton, and L. Stephenson.

Cholesta-1,4-dien-3-one is converted by a mixture of an alcohol, ethyl orthoformate, and sulphuric acid into the 1-alkoxy-4-methyl-19-norcholesta-1,3,5(10)-triene and, in smaller amount, the 3-alkoxy-1-methyl-19-norcholesta-1,3,5(10)-triene.

The acid-catalysed reaction of ethyl orthoformate with saturated 3-oxo-steroids gives diethyl ketals, which can be converted by pyrolysis into enol ethers;[2a] under similar conditions, Δ^4-3-oxo-compounds yield the enol ethers (I) directly.[2] We hoped that a $\Delta^{1,4}$-3-ketone might give the analogous 3-ethoxy-$\Delta^{1,3,5}$-compound (II), but neither prednisone acetate (21-acetoxy-17-hydroxypregna-1,4-diene-3,11,20-trione) nor cholesta-1,4-dien-3-one (III) was affected by treatment with ethyl orthoformate and sulphuric acid in dioxan under conditions known to convert Δ^4-3-ketones into their enol ethers.[2b] However, if the dioxan was replaced by ethanol, cholesta-1,4-dien-3-one yielded an oil showing neither the absorption maximum at 242 mμ of the starting material nor that at ~300 mμ which would be expected of a compound of type (II). Chromatography on alumina split the material into two fractions, neither of them crystalline; the ultraviolet spectrum of each showed a weak band at ~280 mμ, but in the infrared the major fraction showed a strong band at 794 cm.$^{-1}$, whereas the minor fraction showed a band at 852 cm.$^{-1}$. The infrared



(I) (II) (III) (IV) (V)

spectrum of each compound also showed bands attributable to an ether, although the major product was not cleaved under the conditions of the Zeisel alkoxyl determination, and the other gave a very low value.

Acid-catalysed aromatisation of steroid $\Delta^{1,4}$-3-ketones is known to proceed by two paths; under the conditions most commonly used (*i.e.*, a strong-acid catalyst in an acid anhydride), the sole product is the 1-acyloxy-4-methyl-compound [3] (*i.e.*, type IV) * unless the steroid also contains a 6,7-double bond, when the 3-acyloxy-1-methyl-compound (type V) results [4] (see also following paper). However, treatment of androsta-1,4-diene-3,17-dione with concentrated aqueous hydrogen bromide or hydrogen chloride gives a mixture of the "*para*"-phenol (cf. IV; R = H) and the "*meta*"-phenol (cf. V; R = H), in which the latter predominates.[5] It seemed probable that our reaction was giving a mixture of the two types of phenol, as their ethyl ethers, since the absorption of the two products in the 800—850 cm.$^{-1}$ region was consistent with the major and minor products'

* The earlier literature incorrectly ascribes the 3-acyloxy-1-methyl-structure (V) to such compounds.

[1] Part II, Green and Long, *J.*, 1961, 2532.

[2] (*a*) Fieser and Fieser, "Steroids," Reinhold Publ. Corp., New York, 1959, p. 310; (*b*) Meystre and Miescher, *Helv. Chim. Acta*, 1949, **32**, 1758; Sarett, Feurer, and Folkers, *J. Amer. Chem. Soc.*, 1951 **73**, 1777; Julian, Meyer, Karpel, and Cole, *ibid.*, p. 1982; Engel and Just, *ibid.*, 1954, **76**, 4909; Patel, Petrow, Royer, and Stuart-Webb, *J.*, 1952, 161.

[3] Woodward and Singh, *J. Amer. Chem. Soc.*, 1950, **72**, 494; Woodward, Inhoffen, Larson, and Menzel, *Chem. Ber.*, 1953, **86**, 594; Dreiding and Voltman, *J. Amer. Chem. Soc.*, 1954, **76**, 537.

[4] Djerassi, Rosenkranz, Romo, Pataki, and Kaufmann, *J. Amer. Chem. Soc.*, 1950, **72**, 4540; Dreiding and Pummer, *ibid.*, 1953, **75**, 3162.

[5] Dreiding, Pummer, and Tomasewski, *J. Amer. Chem. Soc.*, 1953, **75**, 3159.

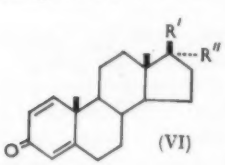
XUM

being 1-ethoxy-4-methyl- (IV; R = Et) and 3-ethoxy-1-methyl-19-norcholesta-1,3,5(10)-triene (V; R = Et), respectively.[5,6] Since the "*para*-compound" (IV; R = Et) could not readily be converted into the known 4-methyl-19-norcholesta-1,3,5(10)-trien-1-ol [7] (IV; R = H) (see above), this phenol was treated with diethyl sulphate, to give its ethyl ether (IV; R = Et), whose spectra and rotation were identical with those of the major product of our ethyl orthoformate reaction. The structure of the isomer (V; R = Et) rests upon its infrared spectrum and rotation (see below).

In the same way, treatment of cholesta-1,4-dien-3-one (III) with ethyl orthoformate and sulphuric acid in methanol gave as the major product the known 1-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (IV; R = Me);[7] the minor one is assigned the "*meta*"-structure (V; R = Me) on reasoning similar to that applied to the ethoxy-compound.

A method that has commonly been used to protect saturated 3-oxo- and Δ^4-3-oxo-steroids involves their conversion into the cyclic ethylene ketals, the double bond in the latter compounds moving to the 5,6-position. When cholesta-1,4-dien-3-one (III) was treated with toluene-*p*-sulphonic acid in ethylene glycol at *ca.* 100° under reduced pressure,[8] the product was again seen from its infrared and ultraviolet spectra to have been aromatised. Chromatography yielded two fractions whose analyses, rotations, and spectra were consistent with their being the hydroxyethoxy-compounds (IV and V; R = $HO{\cdot}CH_2{\cdot}CH_2$). A similar mixture resulted from treatment of the dienone (III) with ethyl orthoformate and sulphuric acid in ethylene glycol at 100° at atmospheric pressure; in the absence of ethyl orthoformate the dienone was unaffected.

In the Table are shown the changes in molecular rotation accompanying the conversion of $\Delta^{1,4}$-3-ketones into known 3-methoxy-1-methyl- and 1-methoxy-4-methyl-$\Delta^{1,3,5}$-compounds; the values for the two types are distinct. The corresponding values for the ethers described in this paper, given in the lower half of the Table [where formulæ (VI) are as inset here], are in good agreement, thus supporting the structures proposed.



(VI)

Two groups of workers [9] have reported their failure to prepare ketals from $\Delta^{1,4}$-3-ketones but they apparently did not observe aromatisation of ring-A under their conditions. Against this, Hogg and his co-workers have referred in a note [10] and in patents [11] to the protection of the $\Delta^{1,4}$-3-oxo-grouping of methyl 3,11-dioxopregna-1,4,17(20)-trien-21-oate as its cyclic ethylene ketal; however, the lack of detail in these publications makes it difficult to comment upon them.

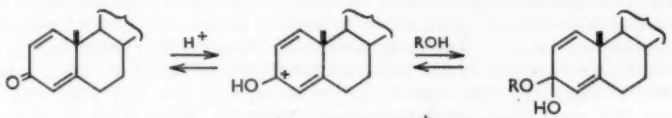
			(VI)	(V)		(IV)	
R *	R′	R″	$[M]_D$	$[M]_D$	$\Delta[M]_D$	$[M]_D$	$\Delta[M]_D$
Me	C_8H_{17}	H	+115° [a]			+713° [b]	+598°
Me	:O		+338 [a]	+710° [c]	+372°	+885 [a]	+547
Me	COMe	H	+374 [d]	+678 [e]	+304		
Me	COMe	OH	+126 [a]	+404 [e]	+278		
Me	$CO{\cdot}CH_2{\cdot}OAc$	H	+495 [f]			+1060	+565
Me	C_8H_{17}	H	+115 [a]	+448	+333		
Et	C_8H_{17}	H	+115 [a]	+451	+336	+710	+595
$HO{\cdot}CH_2{\cdot}CH_2{\cdot}$	C_8H_{17}	H	+115 [a]	+490	+375	+670	+555

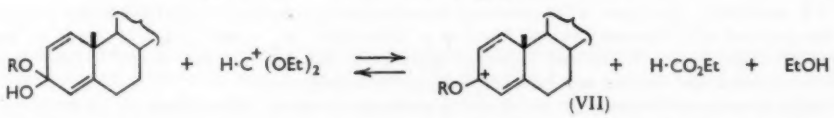
[a] Petit and Mathieu, "Pouvoir Rotatoire Naturel, I. Steroïdes," Masson et Cie., Paris, 1956. [b] This paper. [c] Ringold, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 2477. [d] Sondheimer, Velasco, and Rosenkranz, *J. Amer. Chem. Soc.*, 1955, **77**, 5673. [e] Djerassi, Lippman, and Grossman, *J. Amer. Chem. Soc.*, 1956, **78**, 2479. [f] Vischer, Meystre, and Wettstein, *Helv. Chim. Acta*, 1955, **38**, 835. [g] Djerassi and Scholz, *J. Amer. Chem. Soc.*, 1949, **71**, 3962.

* R is, of course, present only in (IV) and (V), not in (VI).

[6] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 2nd edn., pp. 75—79.
[7] Wilds and Djerassi, *J. Amer. Chem. Soc.*, 1946, **68**, 1712.
[8] Evans, Green, Hunt, Long, Mooney, and Phillipps, *J.*, 1958, 1529; Allen, Bernstein, and Littell, *J. Amer. Chem. Soc.*, 1954, **76**, 6116.
[9] Sondheimer, Velasco, and Rosenkranz, *J. Amer. Chem. Soc.*, 1955, **77**, 5673; Gentles, Moss, Herzog, and Hershberg, *ibid.*, 1958, **80**, 3702.
[10] Hogg, Lincoln, Nathan, Hanze, Schneider, Beal, and Korman, *J. Amer. Chem. Soc.*, 1955, **77**, 4438.
[11] U.S.P. 2,873,271, 2,873,285; B.P. 799,493.

The aromatisation is of some interest in being, we believe, the first example of the direct preparation of phenol ethers by the dienone–phenol rearrangement. As to mechanism, one may invoke a modification of that proposed by MacKenzie and Stocker [12] to explain ketalisation with ethyl orthoformate and an alcohol. The ion (VII), rather than reacting with another molecule of alcohol to give the ketal, or losing a proton to give the enol ether, undergoes the well-understood rearrangement of such ions (in which R = H or acyl) to give the aromatic compounds that we have found.[3,5,13] We, like MacKenzie and Stocker, found (except in the one instance discussed below) that both the alcohol and the orthoformate were required and also that the alkoxy-group in the product was that of the dominant alcohol rather than that associated with the orthoformate molecule.





(VII)

The instance when no ethyl orthoformate was required was special, in that the reaction was carried out under conditions in which water would have been removed as it was formed; the modification (shown below) to the above scheme can reasonably be advanced to deal with this reaction.

Experimental

Rotations and ultraviolet spectra were measured for solutions in chloroform and ethanol, respectively. Infrared spectra were determined in a Perkin–Elmer model 21 spectrophotometer with rock-salt optics. In this and later Parts, assignment of infrared peaks to "*meta*-type" refers to formulæ of type (V) and to "*para*-type" refers to formulæ of type (IV).

1-*Ethoxy*-4-*methyl*- (IV; R = Et) *and* 3-*Ethoxy*-1-*methyl*-19-*norcholesta*-1,3,5(10)-*triene* (V; R = Et).—Cholesta-1,4-dien-3-one (1·0 g.), absolute ethanol (40 ml.), ethyl orthoformate (10 ml.), and concentrated sulphuric acid (0·14 ml.) were boiled together under reflux for 1 hr. The dark red solution was cooled and poured into an excess of aqueous sodium hydrogen carbonate, and the mixture was extracted with ether. The extract was washed, dried ($MgSO_4$), and evaporated under reduced pressure to afford a yellow oil (1·18 g.), $\lambda_{max.}$ 277 mμ ($E^{1\%}_{1\,cm.}$ 46·5). This product was chromatographed on alumina (40 g.) made up in light petroleum (b. p. 40—60°). The first petroleum eluates afforded 1-*ethoxy*-4-*methyl*-19-*norcholesta*-1,3,5(10)-*triene* as a colourless oil (0·60 g., 56%), resistant to crystallisation, having $[\alpha]_D$ +169·5° (*c* 0·7), $\lambda_{max.}$ 277—286 mμ ($E^{1\%}_{1\,cm.}$ 45·2), $\nu_{max.}$ (in CS_2) 1240, 1114, and 1068 (aromatic ether), and 794 $cm.^{-1}$ (*para*-type) (the infrared spectrum resembled that of the authentic material described below) (Found: C, 84·6; H, 11·3; OEt, 0. $C_{29}H_{46}O$ requires C, 84·8; H, 11·3; OEt, 11·0%).

Light petroleum–benzene (9 : 1) eluted 3-*ethoxy*-1-*methyl*-19-*norcholesta*-1,3,5(10)-*triene* as a colourless oil (0·148 g., 14%), resistant to crystallisation, having $[\alpha]_D$ +110° (*c* 0·4), $\lambda_{max.}$ 277—286 mμ ($E^{1\%}_{1\,cm.}$ 51·9), $\nu_{max.}$ (in CS_2) 1300, 1154, and 1054 (aromatic ether), and 852 $cm.^{-1}$ (*meta*-type) (Found: C, 84·2; H, 11·2; OEt, 2·0%).

[12] MacKenzie and Stocker, *J. Org. Chem.*, 1955, **20**, 1695.
[13] Woodward, "Perspectives in Organic Chemistry," ed. Sir Alexander Todd, Interscience Publishers Inc., London, 1956, p. 178.

Preparation of 1-*Ethoxy*-4-*methyl*-19-*norcholesta*-1,3,5(10)-*triene* (IV; R = Et) *from the Corresponding Phenol.*—4-Methyl-19-norcholesta-1,3,5(10)-trien-1-ol [7] (4·4 g.) in ethanol (17 ml.) was warmed and treated alternately with aqueous sodium hydroxide (38% w/w; 1·8 ml.) and diethyl sulphate (2·5 ml.), four additions of each being made. The mixture was set aside for 15 min., water was added, and the mixture was extracted with ether. The extract was washed, dried ($MgSO_4$), and evaporated to dryness under reduced pressure. The oily product (0·51 g.) was dissolved in light petroleum (b. p. 40—60°) and filtered through alumina (10 g.); evaporation of the eluate gave 1-ethoxy-4-methyl-19-norcholesta-1,3,5(10)-triene as a colourless oil (0·36 g.), $[\alpha]_D$ +173° (*c* 1·0), $\lambda_{max.}$ 278—285 mμ ($E^{1\%}_{1\,cm.}$ 43·6) (Found: C, 84·8; H, 11·1; OEt, 0%).

1-*Methoxy*-4-*methyl*- (IV; R = Me) *and* 3-*Methoxy*-1-*methyl*-19-*norcholesta*-1,3,5(10)-*triene* (V; R = Me).—Cholesta-1,4-dien-3-one (1·0 g.), anhydrous methanol (40 ml.), ethyl orthoformate (10 ml.), and concentrated sulphuric acid (0·14 ml.) were boiled together under reflux for 1½ hr. The product was worked up as above to yield a yellow oil (1·09 g.) which was chromatographed on alumina (40 g.). The early petroleum fractions, on crystallisation from methanol, gave 1-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (0·58 g., 56%), m. p. 99—100°, $[\alpha]_D$ +180° (*c* 1·0), $\lambda_{max.}$ 278—285 mμ ($E^{1\%}_{1\,cm.}$ 48·5), $\nu_{max.}$ (in CS_2) 1242 and 1080 (aromatic ether) and 795 cm.$^{-1}$ (*para*-type) (Found: C, 84·7; H, 11·2; OMe, 0. Calc. for $C_{28}H_{44}O$: C, 84·8; H, 11·2; OMe, 7·8%).

An authentic specimen of 1-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene, prepared by the method of Wilds and Djerassi,[7] had m. p. 104—105°, $[\alpha]_D$ +180° (*c* 1·0) (Found: C, 84·5; H, 11·2; OMe, 0%). Wilds and Djerassi [7] give m. p. 104·5—105°, $[\alpha]_D$ +165°. Its infrared spectrum resembled that of material prepared as described above

Light petroleum–benzene (9 : 1) eluted 3-methoxy-1-methyl-19-norcholesta-1,3,5(10)-triene as a colourless oil, resistant to crystallisation, having $[\alpha]_D$ +113° (*c* 0·6), $\lambda_{max.}$ 279 mμ ($E^{1\%}_{1\,cm.}$ 45), $\nu_{max.}$ (in CS_2) 1300, 1145, and 1060 (aromatic ether), and 852 cm.$^{-1}$ (*meta*-type).

Treatment of Cholesta-1,4-*dien*-3-*one with Ethylene Glycol.*—Cholesta-1,4-dien-3-one (1·0 g.), ethylene glycol (40 ml.), and toluene-*p*-sulphonic acid (4 mg.) were boiled together under reflux at 20 mm. pressure for 20 hr. The cooled product was poured into aqueous sodium hydrogen carbonate, and the mixture was extracted with ether. The extract was washed, dried ($MgSO_4$), and evaporated and the residual oil (1·1 g.) was chromatographed on alumina (50 g.). Ether eluted 1-2′-*hydroxyethoxy*-4-*methyl*-19-*norcholesta*-1,3,5(10)-*triene* (0·76 g.) which, after treatment with charcoal, gave a colourless oil, $[\alpha]_D$ +157° (*c* 1·0), $\lambda_{max.}$ 278—285 mμ ($E^{1\%}_{1\,cm.}$ 44), $\nu_{max.}$ (in CS_2) 3620 and 1052 (OH), 1236 and 1080 (aromatic ether), and 794 cm.$^{-1}$ (*para*-type) (Found: C, 81·45; H, 11·2. $C_{29}H_{46}O_2$ requires C, 81·6; H, 10·9%). Chloroform eluted 3-2′-*hydroxyethoxy*-1-*methyl*-19-*norcholesta*-1,3,5(10)-*triene* as an oil (0·18 g.), $[\alpha]_D$ +115° (*c* 0·8), $\lambda_{max.}$ 278—285 mμ ($E^{1\%}_{1\,cm.}$ 34), $\nu_{max.}$ (in CS_2) 3620 and 1050 (OH), 1300, 1150, and 1050 (aromatic ether), and 850 cm.$^{-1}$ (*meta*-type) (Found: C, 81·2; H, 11·0%).

Treatment of Cholesta-1,4-*dien*-3-*one with Ethylene Glycol and Ethyl Orthoformate.*—A mixture of cholesta-1,4-dien-3-one (0·1 g.), ethylene glycol (3 ml.), ethyl orthoformate (1 ml.), and concentrated sulphuric acid (0·015 ml.) was heated at 100° for 1 hr. The cooled solution was worked up as above to give an oil (0·11 g.), $\lambda_{max.}$ 278—285 mμ ($E^{1\%}_{1\,cm.}$ 39), whose infrared spectrum was similar to that of the mixture obtained as described above.

Repetition of this experiment, but with the omission of ethyl orthoformate, gave unchanged cholesta-1,4-dien-3-one.

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX. [*Received, February* 23*rd*, 1961.]

893. *Compounds Related to the Steroid Hormones. Part IV.*[1] *Dienone–Phenol Rearrangement of Steroid* $\Delta^{1,4}$-3,11-*Diketones.*

By (Miss) E. J. Bailey, J. Elks, J. F. Oughton, and L. Stephenson.

Prednisone acetate undergoes aromatisation of ring A on treatment with strong acids in acetic anhydride; the reaction is unusual in giving the 3-acetoxy-1-methyl- rather than the 1-acetoxy-4-methyl-$\Delta^{1,3,5(10)}$-compound. Under mild conditions the 17α-hydroxyl group is acetylated, but the 11-oxo-group is unaffected; under more vigorous conditions, the latter group is enol-acetylated, and hydrolysis then gives the 9β-11-ketone as major product. The structures of these compounds were proved by degradation to the known 3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one.

Aromatisation of androsta-1,4-diene-3,11,17-trione also gives the "*meta*-substituted" product, but the 11β-hydroxy-compound, prednisolone acetate, gives the normal "*para*-substituted" product.

The influence of the 11-oxo-group on the direction of rearrangement is discussed.

The nature of the dienone–phenol rearrangement is now well understood, and the influence of a number of structural features upon its direction has been elucidated. With steroid $\Delta^{1,4}$-3-ketones, in particular, rearrangement in acid anhydrides containing a strong-acid catalyst gives exclusively the 1-acyloxy-4-methyl compound; $\Delta^{1,4,6}$-3-ketones, on the other hand, give the 1-methyl-3-acyloxy-compounds (for references, see the preceding paper, where the effect of other reaction conditions is also discussed). There is, however, no record of the acid-catalysed aromatisation of a steroid $\Delta^{1,4}$-3-ketone containing an oxygen group at position 11, and Kirk, Patel, and Petrow[2] failed to aromatise some $\Delta^{1,4}$- and $\Delta^{1,4,6}$-3,11-diketones under the conditions commonly used for analogous compounds having no 11-substituent.

A recent paper by the same authors[3] describes the conversion, under rather vigorous acidic conditions, of a $\Delta^{1,4,6}$-3,11-diketone into a compound that was believed to be the 3-hydroxy-1-methyl-$\Delta^{1,3,5(10),6}$-11-ketone, but the yield was low and the product was inadequately characterised. Analogous 11α- and 11β-acetoxy-compounds, on the other hand, were rearranged smoothly to the usual type of product.

We have now found that the $\Delta^{1,4}$-3,11-diketone, prednisone acetate (I), does in fact undergo aromatisation when treated in acetic anhydride with sulphuric acid, perchloric acid, or toluene-*p*-sulphonic acid. The course of the reaction was followed by examination of the ultraviolet spectrum of material isolated at intervals; the peak at 238 mμ, characteristic of the $\Delta^{1,4}$-3-ketone chromophore, diminished to a minimum value ($E^{1\%}_{1\,cm.}$ 40—50) and was then replaced by a gradually increasing peak at about 240 mμ. We have not found means to stop the reaction precisely at the intermediate stage, but by use of a low concentration (0·05%) of perchloric acid and by careful control of the reaction time, we have isolated the pure intermediate product in 60% yield.

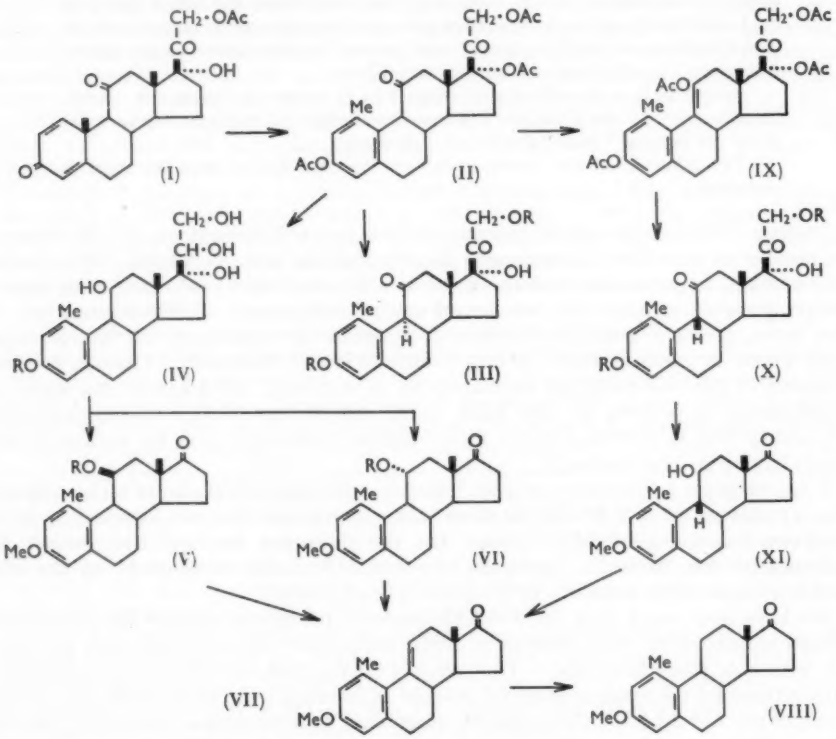
This compound, like its hydrolysis products described below, showed an infrared band close to 850 cm.$^{-1}$, suggestive of a 1,2,3,5- rather than a 1,2,3,4-tetrasubstituted benzene (cf. preceding paper). The other features of the spectrum and the analysis were consistent with the structure (II), which will be shown to represent the compound. Hydrolysis of the triacetate (II), best with only 2 equivs. of sodium hydroxide in methanol,[4] gave the corresponding triol (III; R = H), which showed the expected weak absorption band at ~280 mμ. Acetylation of this compound with acetic anhydride and pyridine at room

[1] Part III, preceding paper.
[2] Kirk, Patel, and Petrow, *J.*, 1957, 1046.
[3] Kirk and Petrow, *J.*, 1960, 4664.
[4] Cf. Ringold, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 820.

XUM

temperature then gave the 3,21-diacetate (III; R = Ac); this reacted with acetic anhydride in the presence of perchloric acid to yield the original triacetate (II).

That the dihydroxyacetone side-chain had remained intact was shown by a triphenyltetrazolium assay on the diacetate (III; R = Ac). [The triacetate (II) showed only some 26% of the calculated value in this analysis, but we have found similarly low figures to be given by other 17α,21-diacetoxy-20-oxo-steroids.] The triacetate (II) could be converted into an enol acetate (IX) whose ultraviolet spectrum showed the new double bond to be conjugated with the aromatic ring (see below); this suggested that there had been no ring rearrangement.



There were thus left undecided only the positions of the methyl and acetoxy-groups in ring A. Confirmation that they were in the *meta*-relationship was provided by bromination experiments, carried out by Dr. W. C. Taylor at Imperial College and already described by him.[5] Final proof that the aromatic compounds were of the 3-hydroxy-1-methyl type came from the degradation shown in the Chart.

Successive treatment of the triacetate (II) with (*a*) lithium aluminium hydride in tetrahydrofuran, (*b*) dimethyl sulphate, and (*c*) sodium metaperiodate gave a mixture of roughly equal amounts of 11β- (V; R = H) and 11α-hydroxy-3-methoxy-1-methyl-œstra-1,3,5(10)-trien-17-one (VI; R = H), each of which formed a methanesulphonate under normal conditions. Treatment of either of these sulphonic esters (V and VI; R = $Me{\cdot}SO_2$) with sodium acetate in boiling acetic acid produced 3-methoxy-1-methyl-œstra-1,3,5(10),9(11)-tetraen-17-one (VII), which gave, on hydrogenation with a palladium

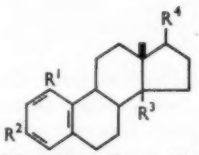
[5] Barton and Taylor, *J.*, 1958, 2500.

catalyst, 3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (VIII), identical with an authentic sample prepared by the method of Dreiding, Pummer, and Tomasewski.[6]

Certain features of this degradation appear worthy of comment. The formation of similar amounts of 11α- and 11β-hydroxy-compounds by reducing an 11-ketone with lithium aluminium hydride contrasts with the usual preponderance of the 11β-epimer. However, models show that, with the aromatisation of ring A and the concomitant shift of the angular methyl group from $C_{(10)}$ to $C_{(1)}$, the hindrance to approach to $C_{(11)}$ from the β-face is greatly reduced; rather the α-face appears the more hindered.

Again, the ready formation of methanesulphonates by both 11-epimers is unusual, in light of the resistance of normal 11β-hydroxy-groups to acylation. A model of the system shows that, if ring B is in the semi-chair form, the 11β-hydroxy-group is not unduly hindered, but that the 11α-hydroxy-group suffers severe hindrance from the 1-methyl group, to the extent that formation of a methanesulphonate would appear difficult. This could be overcome if ring B were to adopt a semi-boat form.

TABLE 1.



					$[M]_D$ *			$\Delta[M]_D$	
R^1	R^2	R^3	R^4	Parent	11-Oxo	11α-OH	11β-OH	11-Oxo	11α-OH	11β-OH
H	HO	α-H	:O	+440° [a] †			+555° [b] †			+115°
H	AcO	α-H	:O	+431 [a]			+630 [b]			+199
H	HO	α-H	β-OH	+215 [a] †		−181° [c] ‡	+372 [d] †		−396°	+157
H	HO	β-OH	β-CO_2H	+253 [e] §	+770° [e] §			+517°		
H	MeO	β-OH	β-CO_2Me	+334 [e]	+967 [e]			+633		
Me	MeO	α-H	β-COMe	+679 [f]	+1261 [g]	−192 [g]		+582	−871	
Me	HO	α-H	β-OH	+418 [a]			+33 [g]			−385
Me	HO	α-H	:O	+730 [a]	+1269 [h] ‡			+539		
Me	AcO	α-H	:O	+730 [a]	+1274 [h]			+544		
Me	MeO	α-H	:O	+709 [i]		−166 [h]	+754 [h]		−875	+45

[a] Petit and Mathieu, "Pouvoir Rotatoire Naturel, I. Stéroïdes," Masson et Cie., Paris, 1956. [b] Magerlein and Hogg, *J. Amer. Chem. Soc.*, 1958, **80**, 2220. [c] *Idem, ibid.*, 1957, **79**, 1508. [d] *Idem, ibid.*, 1958, **80**, 2226. [e] Tamm, Volpp, and Baumgartner, *Helv. Chim. Acta*, 1957, **40**, 1469. [f] Djerassi, Lippmann, and Grossman, *J. Amer. Chem. Soc.*, 1956, **78**, 2479. [g] Kirk and Petrow, *J.*, 1960, 4664. [h] This paper. [i] Ringold, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 2477.

* In $CHCl_3$ unless otherwise stated. † In dioxan. ‡ In acetone. § In methanol.

In Table 1 there are set out the molecular rotation contributions of 11-oxo- and 11α- and 11β-hydroxy-groups in 3-oxy-$\Delta^{1,3,5}$-steroids; the last three lines refer to the compounds described in this paper. The value for an 11-oxo-group is rather consistent, the presence or absence of a 1-methyl group having no obvious effect; it is, however, very much greater than the standard value (+79°) given for steroids in which ring A is not aromatic (cf. ref. *e*). Agreement is less good among the 11-hydroxy-compounds, but there are too few examples to make an analysis profitable; however, an 11α-hydroxy-group makes a large negative contribution to the molecular rotation and, with one exception, an 11β-hydroxy-group makes a modest positive contribution. It seems justifiable, therefore, to differentiate between our isomeric 11-hydroxy-compounds (V and VI; R = H) on the basis of their widely different rotations, which do, in fact, fit into the general pattern of Table 1 (see last line).

The tetraenone (VII) had its main maximum in the ultraviolet region at a rather lower wavelength (253 mμ) than would be expected; analogous $\Delta^{1,3,5(10),9(11)}$-tetraenones, unmethylated at $C_{(1)}$, absorb, as do $\Delta^{1,3,5(10),6}$-tetraenones, at *ca.* 264 mμ.[7] This hypsochromic

[6] Dreiding, Pummer, and Tomasewski, *J. Amer. Chem. Soc.*, 1953, **75**, 3159.
[7] Dorfman, *Chem. Rev.*, 1953, **53**, 47.

effect presumably arises from the interaction between the 11-hydrogen atom and the 1-methyl group, with a consequent departure from planarity of the styrene chromophore. Dodson and Muir [8] have recently given the $\lambda_{max.}$ for 1-hydroxy-4-methylœstra-1,3,5(10),9(11)-tetraen-17-one as 255·5 mμ and a similar effect is probably operating here.

It will be noted that reduction of the 9,11-double bond in the tetraenone (VII) proceeded mostly by rear-side attack. However, the crude hydrogenation product was clearly a mixture and may well have contained the 9β-epimer of the major product (VIII). The formation of the 8β,9α-compound (VIII) rules out, incidentally, the possibility that the tetraenone had the $\Delta^{1,3,5(10),8(9)}$-structure if *cis*-addition of hydrogen is assumed.

To return to the aromatisation of prednisone acetate (I), prolonged treatment, in acetic anhydride, with sulphuric acid at room temperature or with toluene-*p*-sulphonic acid at 100° gave a non-crystalline material with $\lambda_{max.}$ 242 mμ, $E^{1\%}_{1\,cm.}$ *ca.* 250; the same product was obtained, along with the triacetate (II), when the rearrangement was carried out with *ca.* 0·1% perchloric acid in acetic anhydride. The infrared spectrum suggested that enol acetylation of the 11-ketone group had occurred and this was confirmed by analysis for acetyl, which indicated a tetra-acetoxy-compound. The $\lambda_{max.}$, though apparently low for structure (IX) may, perhaps, be again explained by distortion of the styrene chromophore.

Gentle hydrolysis of the tetra-acetate (IX), with subsequent reacetylation, gave the expected compound (III; R = Ac) as a minor product only, the major product being an isomer thereof. A close structural relationship between the compounds was suggested by their spectra and by the fact that treatment of the triacetate (II) with acetic anhydride containing sulphuric acid gave the enol acetate (IX) and thence the new isomer. These experiments pointed to $C_{(9)}$ as the centre of isomerism, and proof of this came from a degradation of the isomer (X; R = Ac) similar to that applied to the triacetate (II). In this instance, the two 11-hydroxy-17-ketones (XI) could not be completely separated, but successive treatment of the mixture with methanesulphonyl chloride–pyridine and sodium acetate–acetic acid gave 3-methoxy-1-methylœstra-1,3,5(10),9(11)-tetraen-17-one (VII), identical with the material obtained as already described.

The material arising *via* the enol acetate is, then, the 9β-epimer (X) of compound (III). Its occurrence as the major product of hydrolysis of the enol acetate shows that this B/C-*cis*-fused compound is of the same order of stability as the *trans*-fused epimer. This contrasts strongly with the situation in steroids (at least in the 5α-series) in which ring A is saturated, when the equilibrium is greatly in favour of the 9α-form.[9] However, it is made less surprising by a number of observations in recent years, that in 1,2,3,4,9,10,11,12-octahydrophenanthrenes, *cis*- and *trans*-fusion of the non-aromatic rings may confer similar stability;[10] the effect of the aromatic ring in increasing the stability of the *cis*-forms has been plausibly explained on conformational grounds.

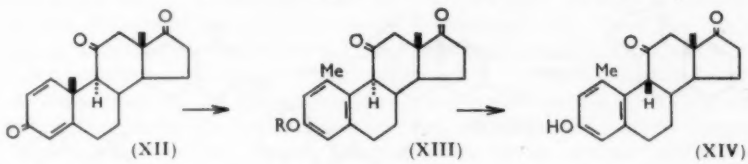
Direct interconversion of compounds (III) and (X) has been tried with perchloric acid in acetic acid. Rotational and paper-chromatographic studies suggested that a mixture of the isomers was obtained from either of them, but an attempt to isolate the 9β-isomer after such treatment of the 9α-compound was only partly successful.

Androsta-1,4-diene-3,11,17-trione [5,11] (XII), on treatment with 0·1% perchloric acid in acetic anhydride for 6 hr., gave 3-acetoxy-1-methylœstra-1,3,5(10)-triene-11,17-dione (XIII; R = Ac); neither the 11- nor the 17-ketone group was enol-acetylated. (With longer reaction times, increasing absorption at 242 mμ indicated enol-acetylation of the

[8] Dodson and Muir, *J. Amer. Chem. Soc.*, 1958, **80**, 5004.
[9] Bladon, Henbest, Jones, Lovell, Wood, Woods, Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921.
[10] Reusch, Ph.D. Diss., Columbia, 1957; Barltrop and Rogers, *J.*, 1958, 2566; Wenkert and Stevens, *J. Amer. Chem. Soc.*, 1956, **78**, 2318; Johnson, David, Dehm, Highet, Warnhoff, Wood, and Jones, *ibid.*, 1958, **80**, 661; Wenkert and Chamberlin, *ibid.*, 1959, **81**, 688; Saha, Ganguly, and Dutta, *ibid.*, p. 3670; Birch, Smith, and Thornton, *J.*, 1957, 1339.
[11] Herzog, Payne, Jevnik, Gould, Shapiro, Oliveto, and Hershberg, *J. Amer. Chem. Soc.*, 1955, **77**, 4781.

11-oxo-group.) The structure assigned to this compound rests on its infrared spectrum and that of the corresponding 3-hydroxy-compound (XIII; R = H), which were in favour of a " *meta-* " rather than a " *para*-substituted " type.

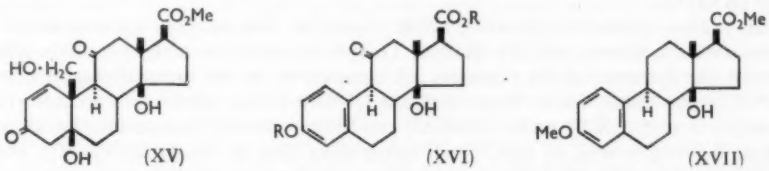
Treatment of the acetate (XIII; R = Ac) with either acid or base caused changes in the rotation and infrared spectrum suggestive of epimerisation at $C_{(9)}$, but the reactions



(XII) (XIII) (XIV)

were not clean, and it was only with difficulty that a relatively pure specimen of the presumed 9β-compound (XIV) could be isolated.

Tamm, Volpp, and Baumgartner [12] obtained, by the gentle action of alkali upon methyl 5,14,19-trihydroxy-3,11-dioxo-5β,14β-androst-1-ene-17β-carboxylate (XV), with subsequent esterification and 3-*O*-methylation, methyl 14-hydroxy-3-methoxy-11-oxo-14β-œstra-1,3,5(10)-triene-17β-carboxylate (XVI; R = Me); under more vigorous alkaline



(XV) (XVI) (XVII)

conditions an isomer was obtained, and no structure was assigned to it: in the light of our observation of the stability of 9β-11-ketones in the aromatic-A series, a likely structure is that of the 9β-epimer of compound (XVI; R = Me). Again, Wolff–Kishner reduction of the 11-ketone (XVI; R = H) and subsequent treatment with diazomethane gave methyl 14-hydroxy-3-methoxy-14β-œstra-1,3,5(10)-triene-17β-carboxylate (XVII) together with an isomer, which was regarded as the 17α-epimer; since equilibrium could well be established at $C_{(9)}$ before reduction, the isomer may as likely be the 9β-epimer of (XVII). In Table 2 is shown the change in molecular rotation associated with epimerisation at $C_{(9)}$ in our compounds, together with the differences between the isomers described by Tamm *et al.*; [12] though agreement is only partial, the rotation results by no means exclude the above suggestion.

TABLE 2.

Compound	$[M]_D$	$\Delta[M]_D$	Compound	$[M]_D$	$\Delta[M]_D$
(III; R = Ac)	+1184°	−649°	(XVI; R = Me)	+967° [12]	−318°
(X; R = Ac)	+535		Isomer	+649 [12]	
(XIII; R = H)	+1270 *	−549	(XVII)	+334 [12]	−327
(XIV)	+721 *		Isomer	+7 [12]	

* In acetone

The dienone–phenol rearrangement is considered to proceed as annexed (ref. 13; see also preceding paper).

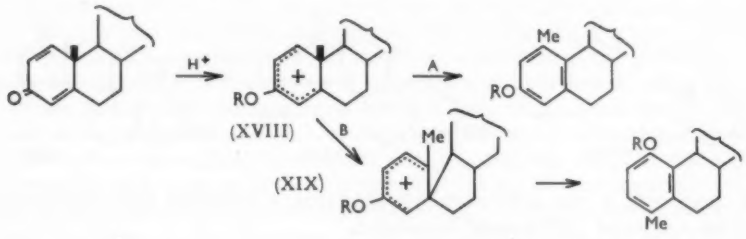
With a simple 1,4-dien-3-one, saturated and unsubstituted in rings B and C, pathway B, involving migration of a tertiary carbon atom, is preferred to pathway A, in which a methyl group migrates. The effect of a 6,7-double bond in favouring pathway A has

[12] Tamm, Volpp, and Baumgartner, *Helv. Chim. Acta*, 1957, **40**, 1469.

[13] (*a*) Woodward and Singh, *J. Amer. Chem. Soc.*, 1950, **72**, 494; (*b*) Woodward, " Perspectives in Organic Chemistry," ed. Sir Alexander Todd, Interscience Publ. Inc., London, 1956, p. 178; (*c*) Djerassi, Rosenkranz, Romo, Pataki, and Kaufmann, *J. Amer. Chem. Soc.*, 1950, **72**, 4540.

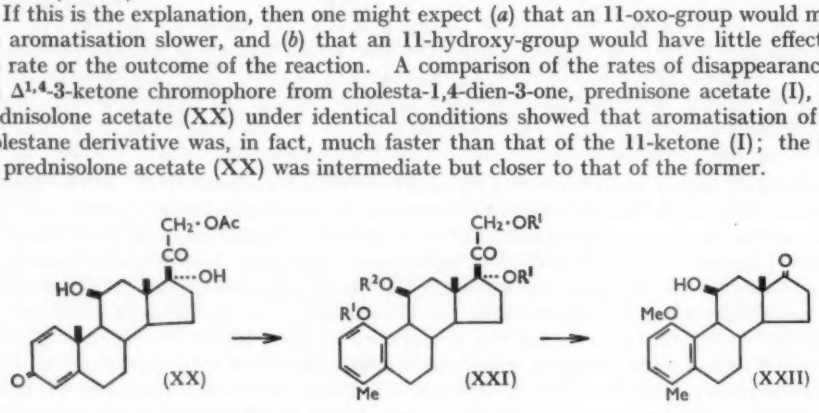
XUM

been attributed [13c] to the 5,6-bond in the intermediate ion (XVIII) having some double-bond character, which inhibits formation of the spiro-intermediate (XIX). The effect we have now demonstrated, of an 11-oxo-group in favouring pathway A, presumably results from inhibition of migration of $C_{(9)}$, due to the electron-withdrawing effect of the



neighbouring carbonyl group. Another factor that would tend to the same result and may also be important is the proximity of the negative end of the 11-carbonyl dipole to $C_{(1)}$, which would tend to stabilise the positive charge on that carbon atom in the intermediate (XVIII).

If this is the explanation, then one might expect (*a*) that an 11-oxo-group would make the aromatisation slower, and (*b*) that an 11-hydroxy-group would have little effect on the rate or the outcome of the reaction. A comparison of the rates of disappearance of the $\Delta^{1,4}$-3-ketone chromophore from cholesta-1,4-dien-3-one, prednisone acetate (I), and prednisolone acetate (XX) under identical conditions showed that aromatisation of the cholestane derivative was, in fact, much faster than that of the 11-ketone (I); the rate for prednisolone acetate (XX) was intermediate but closer to that of the former.



The speed of aromatisation of prednisolone acetate (XX) was such that it was not possible to acetylate the 17α-hydroxy-group without concurrent rearrangement in ring A. There was no great tendency towards elimination of the 11β-hydroxy-group, although if reaction was prolonged, a band in the ultraviolet spectrum at *ca.* 250 mμ suggested that dehydration was occurring. The product was a mixture that could not be completely separated into its components, but paper chromatography showed two well-separated spots. The infrared spectrum of the mixture showed a band at 810 $cm.^{-1}$, indicative of "*para*-substitution," but none at 850 $cm.^{-1}$, and was consistent with the mixture's consisting of the fully acetylated compound (XXI; $R^1 = R^2 = Ac$) and the triacetate (XXI; $R^1 = Ac$, $R^2 = H$). Mild alkaline hydrolysis of the mixture gave, in poor yield, a single product, analysing as a tetraol monoacetate (XXI; $R^1 = H$, $R^2 = Ac$). These structures for the partly acetylated products are based on the expectation that the 17-hydroxy-group would be acetylated under the aromatisation conditions and regenerated during the alkaline hydrolysis.[14] The nature of the substitution in ring A is based upon the infrared spectrum, and upon the assumption that the rearrangement will follow pathway

[14] Evans, Hamlet, Hunt, Jones, Long, Oughton, Stephenson, Walker, and Wilson, *J.*, 1956, 4356.

B (see Chart), rather than the less probable one leading to the 4-hydroxy-1-methyl derivative, through migration of $C_{(6)}$ in the intermediate (XIX).

An attempt to prove this last point rigidly has been made, albeit unsuccessfully. The mixture obtained by aromatisation of prednisolone acetate (XX) was treated successively with (*a*) lithium aluminium hydride in tetrahydrofuran, (*b*) dimethyl sulphate, and (*c*) sodium metaperiodate. Chromatography gave a very poor yield of a compound with analysis and infrared spectrum in reasonable agreement with those for the expected 11β-hydroxy-1-methoxy-4-methylœstra-1,3,5(10)-trien-17-one (XXII); an unusual feature of the spectrum was a double band at 812 and 798 cm.$^{-1}$. It was hoped that this compound could be dehydrated to the known 1-methoxy-4-methylœstra-1,3,5(10),9(11)-tetraen-17-one,[8] but neither under the conditions used successfully for the similar compounds (V) and (VI), nor under a variety of other dehydrating conditions, was any material produced showing spectroscopic evidence for the formation of the required tetraenone.

Experimental

Rotations were measured with solutions in chloroform unless otherwise specified. The dihydroxyacetone side-chain was estimated by the method of Mader and Buck,[15] with cortisone acetate as standard. For other general information, see preceding paper.

Aromatisation of Prednisone Acetate.—(a) *With 0·05% perchloric acid in acetic anhydride.* Prednisone acetate (10 g.) was dissolved in warm acetic anhydride (290 ml.) and the solution was cooled to room temperature. 60% w/w Aqueous perchloric acid (0·15 ml.) was added dropwise to ice-cold acetic anhydride (9·85 ml.), and the solution was added to the suspension of the steroid, which was then stirred at room temperature. The mixture became clear after 1½ hr. and was then set aside for a further 3¾ hr.; it was poured into aqueous sodium hydrogen carbonate and extracted with ethyl acetate. The extract was washed with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated to dryness, to give material (14·4 g.) with $\lambda_{max.}$ 240 mμ ($E^{1\%}_{1\ cm.}$ 40·8). This product (10·5 g.) was chromatographed on Florisil (100 g.), the column being eluted with benzene containing increasing amounts of ethyl acetate. Crystallisation from ethanol gave 3,17,21-*triacetoxy*-1-*methyl*-19-*norpregna*-1,3,5(10)-*triene*-11,20-*dione* (II) (5·4 g., 61%), m. p. 198—201°, $[\alpha]_D$ +178° (*c* 1·0). The analytical specimen had m. p. 198—200°, $[\alpha]_D$ +177° (*c* 1·0) (Found: C, 66·85; H, 6·55; Ac, 24·1. $C_{27}H_{32}O_8$ requires C, 66·9; H, 6·7; Ac, 26·6%), $\nu_{max.}$ (in Nujol) 1754 and 1198 (aromatic OAc), 1736 and 1266 (21-OAc), 1724 and 1238 (OAc), 1716 (C=O) and 846 cm.$^{-1}$ (*meta*-type). Side-chain assay, 26%; prednisone 17,21-diacetate also gave a value of 26% in the same assay.

(b) *With 0·1% perchloric acid in acetic anhydride.* Prednisone acetate (12·0 g.) in acetic anhydride (300 ml.) was treated with a mixture of 60% w/w aqueous perchloric acid (0·375 ml.) and acetic anhydride (30 ml.) as described above. The solution was left at room temperature for 5 hr. and was then added slowly to a stirred suspension of sodium hydrogen carbonate (650 g.) in water (3 l.). The crude product (16·02 g.), isolated as described above, had $\lambda_{max.}$ 239·5 mμ ($E^{1\%}_{1\ cm.}$ 135). This product (15 g.), in benzene, was chromatographed on alumina (Grade II—III; 400 g.). Benzene eluted 12·2 g. of material which, on crystallisation from ethanol, gave 3,17,21-triacetoxy-1-methyl-19-norpregna-1,3,5(10)-triene-11,20-dione (II) (2·39 g., 18%), m. p. 190—197°. Evaporation of the ethanol mother-liquors gave 7·8 g. of residue, which was chromatographed on Florisil (300 g.). Benzene containing 5% and then 10% of ethyl acetate eluted 4·75 g. (32%) of 3,11,17,21-tetra-acetoxy-1-methyl-19-norpregna-1,3,5(10),9(11)-tetraen-20-one (IX), $\lambda_{max.}$ 242·5 mμ ($E^{1\%}_{1\ cm.}$ 260). Benzene containing 15% and then 25% of ethyl acetate eluted 2·39 g. of material which, on crystallisation from ethanol, gave a further 1·59 g. (12%) of 3,17,21-triacetoxy-1-methyl-19-norpregna-1,3,5(10)-triene-11,20-dione, m. p. 194—197°.

A similar experiment, carried out for 24 hr., gave a crude product with $\lambda_{max.}$ 243 mμ ($E^{1\%}_{1\ cm.}$ 219), enol acetylation of the 11-oxo-group being more or less complete.

(c) *With sulphuric acid and acetic anhydride.* Prednisone acetate (1·5 g.) was dissolved in warm acetic anhydride (40 ml.). The solution was cooled to room temperature and treated with a solution of sulphuric acid (0·1 ml.) in acetic anhydride (3 ml.). After being left at room temperature for 2 hr., the solution was treated with a further quantity of sulphuric acid

[15] Mader and Buck, *Analyt. Chem.*, 1952, **24**, 666.

(0·2 ml.) in acetic anhydride (3 ml.) and left for a further 16 hr. It was worked up as above, to give material (1·52 g.) with $\lambda_{max.}$ 240—242 mμ ($E^{1\%}_{1\,cm.}$ 225). This product was chromatographed on alumina (Grade II; acid-washed; 70 g.). Benzene eluted **3,11,17,21-*tetra-acetoxy*-1-*methyl*-19-*norpregna*-1,3,5(10),9(11)-*tetraen*-20-*one*** (IX) as an oil (0·90 g., 46%), $\lambda_{max.}$ 242 mμ $E^{1\%}_{1\,cm.}$ 248 (Found: Ac, 33·3. $C_{29}H_{34}O_9$ requires Ac, 32·8%), $\nu_{max.}$ (in Nujol) 1754 and 1210 (aromatic OAc), 1734 and 1234 (OAc) and 840 cm.$^{-1}$ (*meta*-type).

The use of toluene-*p*-sulphonic acid as catalyst is exemplified below.

3,17,21-*Trihydroxy*-1-*methyl*-19-*norpregna*-1,3,5(10)-*triene*-11,20-*dione* (III; R = H).—3,17,21-Triacetoxy-1-methyl-19-norpregna-1,3,5(10)-triene-11,20-dione (2 g.) in methanol (200 ml.) was treated with 2% w/v methanolic potassium hydroxide (23·2 ml.; 2 equiv.) under nitrogen and left at room temperature for ½ hr. Acetic acid was added to neutralise the alkali, followed by water, and the methanol was distilled off under reduced pressure. The white precipitate was filtered off and crystallised from aqueous methanol, giving **3,17,21-*trihydroxy*-1-*methyl*-19-*norpregna*-1,3,5(10)-*triene*-11,20-*dione*** (1·0 g., 68%), m. p. 229—232°, $[\alpha]_D$ +282° (*c* 1·0 in acetone) (Found: C, 70·3; H, 7·6. $C_{21}H_{26}O_5$ requires C, 70·4; H, 7·3%), $\lambda_{max.}$ 278—285 mμ ($E^{1\%}_{1\,cm.}$ 43·7), $\nu_{max.}$ (in Nujol) 3470 and 3300 (OH), 1709 and 1689 (C=O), and 856 cm.$^{-1}$ (*meta*-type). Side-chain, 92%.

3,21-*Diacetoxy*-17-*hydroxy*-1-*methyl*-19-*norpregna*-1,3,5(10)-*triene*-11,20-*dione* (III, R = Ac).—The foregoing triol (0·35 g.) was acetylated overnight at room temperature with pyridine (2·5 ml.) and acetic anhydride (2·5 ml.). The solution was poured into water and the product isolated with ethyl acetate. Crystallisation from ethyl acetate (charcoal) gave the **3,21-*diacetate*** (0·25 g., 58%), m. p. 235—236°, $[\alpha]_D$ +268° (*c* 1·0) (Found: C, 67·7; H, 6·7; Ac, 19·9. $C_{25}H_{30}O_7$ requires C, 67·85; H, 6·8; Ac, 19·4%), $\nu_{max.}$ (in Nujol) 3440 (OH), 1744 and 1210 (aromatic OAc), 1744 and 1240 (21-OAc), 1730 (20-C=O), 1690 (11-C=O) and 848 cm.$^{-1}$ (*meta*-type). Side chain 90%.

3,17,21-*Triacetoxy*-1-*methyl*-19-*norpregna*-1,3,5(10)-*triene*-11,20-*dione* *from the* 3,21-*Di-acetate*.—The foregoing diacetate (0·1 g.) in benzene (2 ml.) was shaken with a 0·125% solution of perchloric acid in acetic anhydride (0·2 ml.) until the solid had dissolved (30 min.) and then for a further ½ hr. It was diluted with benzene and washed successively with water, aqueous sodium hydrogen carbonate, and water, dried ($MgSO_4$), and evaporated. Crystallisation of the residue from ethanol gave the triacetoxy-compound (54 mg., 49%), m. p. 193—195°, undepressed on admixture with a sample prepared as described above. The identity of the compounds was also indicated by their infrared spectra.

Degradation of **3,17,21-*Triacetoxy*-1-*methyl*-19-*norpregna*-1,3,5(10)-*triene*-11,20-*dione*.**—Lithium aluminium hydride (1·6 g.) was added to tetrahydrofuran (freshly distilled from phenylmagnesium bromide; 60 ml.) and stirred under nitrogen for 1 hr. A solution of the steroid (1·57 g.) in tetrahydrofuran (60 ml.) was added and the mixture was boiled under reflux with stirring for 5 hr., then left overnight at room temperature. The excess of hydride was destroyed by ethyl acetate; water and 2N-sulphuric acid were added and the product was isolated with ethyl acetate. The crude mixture of pentaols (IV; R = H) weighed 1·10 g.

The products (1·90 g.) from two such experiments were dissolved in methanol (125 ml.) and the solution was stirred at 30° while dimethyl sulphate (10 ml.) and 40% aqueous sodium hydroxide (5 ml.) were added, each in 5 equal portions, added alternately. Sufficient of the alkali was added to make the solution permanently alkaline and the treatment with dimethyl sulphate and sodium hydroxide was repeated. The alkaline solution was evaporated to small bulk under reduced pressure, the residue was diluted with water, and the product was isolated with ethyl acetate.

The crude mixture of 3-methoxy-11,17,20,21-tetraols (IV; R = Me) (1·91 g.) in ethanol (140 ml.) and water (210 ml.) was treated with sodium metaperiodate (2·8 g.) and left at room temperature for 24 hr. The solution was diluted with water and extracted with ether. Concentration of the extract and storage at room temperature for a few hours resulted in the separation of 11α-hydroxy-3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (VI; R = H) (0·45 g., 26%), m. p. 172—178°, $[\alpha]_D$ −38·4° (*c* 0·89). Evaporation of the filtrate left a froth (1·01 g.), which was chromatographed on acid-washed alumina (grade II—III, 30 g.). The first 1 : 1 hexane–benzene eluate contained material whose infrared spectrum indicated the presence of 11-ketone. Subsequent elution with the same mixture and then with pure benzene gave 11β-hydroxy-3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (V; R = H) (0·583 g.) which, on crystallisation from aqueous methanol, gave 0·361 g. (21%) of material, m. p. 168—173°,

$[\alpha]_D$ +240° (*c* 1·12). Benzene containing 10% and then 25% of ether eluted a further quantity of the 11α-hydroxy-epimer which, on crystallisation from aqueous methanol, gave 0·061 g. (3%) of material, m. p. 174—180°, $[\alpha]_D$ −43° (*c* 1·0).

The analytical specimen of the *11α-hydroxy-compound* (from aqueous acetone) formed prisms, m. p. 176—177°, $[\alpha]_D$ −53° (*c* 0·99) (Found: C, 76·2; H, 8·5. $C_{20}H_{26}O_3$ requires C, 76·4; H, 8·3%), $\nu_{max.}$ (in CS_2) 3620 (OH), 1745 (17-C=O), 1296, 1142, and 1046 (aromatic ether) and 852 cm.$^{-1}$ (*meta*-type).

The *11β-hydroxy-epimer* (Found: C, 76·1; H, 8·1%) melted at 172—174° after crystallisation from aqueous methanol and had $[\alpha]_D$ +240° (*c* 1·2), $\nu_{max.}$ (in CS_2) 3600 (OH), 1745 (17-C=O), 1295, 1142, and 1062 (aromatic ether) and 852 cm.$^{-1}$ (*meta*-type).

A mixture of the two epimers melted between 150° and 178°.

3-Methoxy-1-methylœstra-1,3,5(10),9(11)-tetraen-17-one (VII).—*From 11β-hydroxy-3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one.* To the steroid (150 mg.), in chloroform (3 ml.) containing pyridine (0·6 ml.), was added methanesulphonyl chloride (0·3 ml.), with shaking at 0° during 5 min. The mixture was left overnight in the refrigerator, treated with ice, and extracted with chloroform, to give the crude 11β-methanesulphonate (218 mg.). This material (207 mg.) was boiled under reflux for ½ hr. with a mixture of freshly fused sodium acetate (600 mg.) and acetic acid (6 ml.). Water was added and the product was isolated with ether. The residual gum (141 mg.), which partly crystallised, was chromatographed on alumina (acid-washed; grade I; 5 g.). Hexane–benzene (1 : 1) and benzene eluted 85 mg. of crystals which crystallised from aqueous methanol to give 71 mg. of material which melted at 94—96°. The analytical specimen of the *tetraenone* had m. p. 95—97°, $[\alpha]_D$ +276° (*c* 1·04), $\lambda_{max.}$ 252·5 mμ ($E^{1\%}_{1\,cm.}$ 508) (Found: C, 81·2; H, 8·5. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·2%), $\nu_{max.}$ (in CS_2) 1740 (17-C=O), 1298, 1152, and 1062 (OMe), and 856 cm.$^{-1}$ (*meta*-type).

From 11α-hydroxy-3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one. Treatment of the steroid (250 mg.) with methanesulphonyl chloride as described above gave the crude 11α-methanesulphonyloxy-compound (293 mg.). Treatment of this with sodium acetate and acetic acid as above gave 221 mg. of the crude tetraene which, on chromatography followed by crystallisation from methanol, gave the pure material (125 mg., 53%), m. p. 97—98°, undepressed on admixture with material prepared as described above; it had $\lambda_{max.}$ 253 mμ ($E^{1\%}_{1\,cm.}$ 494). The specimens had identical infrared spectra.

3-Methoxy-1-methylœstra-1,3,5(10)-trien-17-one (VIII).—*By reduction of 3-methoxy-1-methylœstra-1,3,5(10),9(11)-tetraen-17-one.* The tetraenone (86 mg.) in ethyl acetate (15 ml.), containing 10% palladised charcoal (43 mg.), was shaken under hydrogen for 1½ hr. The ultraviolet spectrum of the crude material showed that hydrogenation of the 9,11-double bond was complete in this time. The catalyst was filtered off and the filtrate evaporated to give an oil that rapidly solidified (m. p. 110—121° after preliminary softening). Crystallisation from methanol gave 3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (40 mg., 46%) as prisms, m. p. 125—126°, undepressed on admixture with a sample prepared as described below and having an identical infrared spectrum.

From androsta-1,4-diene-3,17-dione.[6] Androsta-1,4-diene-3,17-dione (0·78 g.) and 48% hydrobromic acid (11 ml.) were heated together in a Carius tube at 55° for 2 days. The mixture was filtered and the dark solid was washed with water and then heated for 3 hr. on the water bath with 5% aqueous sodium hydroxide (170 ml.). The cooled solution was filtered from a little insoluble material and acidified with hydrochloric acid. The precipitated pink solid (0·56 g.), m. p. 200—225°, was seen from its infrared spectrum to contain both the 3-hydroxy-1-methyl and the 1-hydroxy-4-methyl compound. Crystallisation from methanol gave a first crop (0·178 g., 23%), m. p. 249—251°, consisting substantially of 1-methylœstrone (Djerassi *et al.*[13c] give m. p. 250—252°).

1-Methylœstrone (0·17 g.) was methylated with dimethyl sulphate and sodium hydroxide as described above. The crude product (0·164 g.), isolated with ether, was chromatographed on alumina (grade I; acid–washed; 5 g.). Hexane containing 20% and then 50% of benzene eluted 3-methoxy-1-methylœstra-1,3,5(10)-trien-17-one (75 mg., 42%), m. p. 125—126·5° (from methanol), $[\alpha]_D$ +245° (*c* 1·03), $\nu_{max.}$ (in CS_2) 1744 (17-C=O), 1300, 1145, and 1064 (OMe), and 854 cm.$^{-1}$ (*meta*-type) (Ringold *et al.*[18] give m. p. 129—130°, $[\alpha]_D$ +238°).

3,21-Diacetoxy-17-hydroxy-1-methyl-19-nor-9β-pregna-1,3,5(10)-triene-11,20-dione (X; R = Ac).—(a) *From 3,11,17,21-tetra-acetoxy-1-methyl-19-norpregna-1,3,5(10),9(11)-tetraen-20-one.*

[18] Ringold, Rosenkranz, and Sondheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 2477.

XUM

The steroid (4·75 g.) in dry methanol (160 ml.) was treated with 2·44N-methanolic sodium methoxide (14·9 ml.) in an atmosphere of nitrogen. After 4 min., water (0·6 ml.) was added, followed after a further 5 min. by water (60 ml.) and acetic acid (10 ml.). Most of the methanol was removed under reduced pressure and the residue was diluted with water. The product (3·34 g.) was isolated with ethyl acetate and acetylated overnight at room temperature with pyridine (20 ml.) and acetic anhydride (20 ml.). The solution was poured on ice, and the product was isolated with methylene chloride. Trituration of the recovered gum with ethanol gave crystals (1·34 g., 34%), m. p. 187—189°, after a change of crystal form at 155°. The analytical specimen of **3,21-*diacetoxy*-17-*hydroxy*-1-*methyl*-19-*nor*-9β-*pregna*-1,3,5(10)-*triene*-11,20-*dione*** had m. p. 187—189°, $[\alpha]_D$ +121° (*c* 0·7) (Found: C, 67·7; H, 7·0; Ac, 20·6. $C_{25}H_{30}O_7$ requires C, 67·85; H, 6·8; Ac, 19·4%), $\nu_{max.}$ (in Nujol) 3600 and 3400 (OH), 1764 and 1205 (aromatic OAc), 1745 and 1228 (21-OAc), 1728 (20-C=O), 1682 (11-C=O), and 834 cm.$^{-1}$ (*meta*-type). Side-chain assay, 94%.

The alcoholic mother-liquors deposited prisms. Ether was added and the mixture was stored in the refrigerator, to give 3,21-diacetoxy-17-hydroxy-1-methyl-19-norpregna-1,3,5(10)-triene-11,20-dione (0·32 g., 8%), m. p. 232—235°, undepressed on admixture with material prepared as described above and having an identical infrared spectrum and $[\alpha]_D$ +268° (*c* 1·03).

(b) *From prednisone acetate, without isolation of intermediates.* Prednisone acetate (2 g.), acetic anhydride (25 ml.), and toluene-*p*-sulphonic acid (0·5 g.) were heated together at 100° for 4 hr. The solution was cooled and poured into aqueous sodium hydrogen carbonate. Isolation with ethyl acetate gave 2·66 g. of material which was hydrolysed and then reacetylated as described in paragraph (a). The product (2·08 g.) was chromatographed on Florisil (100 g.). Benzene containing up to 10% of ethyl acetate eluted material which, on crystallisation from ethyl acetate–hexane, gave 3,21-diacetoxy-17-hydroxy-1-methyl-19-nor-9β-pregna-1,3,5(10)-triene-11,20-dione (0·72 g., 33%), m. p. 180—184°.

(c) *From* **3,17,21-*triacetoxy*-1-*methyl*-19-*norpregna*-1,3,5(10)-*triene*-11,20-*dione*.** The triacetate (0·5 g.) in acetic anhydride (12 ml.) was left with sulphuric acid (0·125 ml.) in acetic anhydride (3 ml.) at room temperature for 20 hr. Addition to aqueous sodium hydrogen carbonate and isolation with ethyl acetate gave the tetra-acetoxy-compound (IX) (0·49 g.), $\lambda_{max.}$ 243 mμ ($E^{1\%}_{1\ cm.}$ 233). Hydrolysis, acetylation, and isolation as above gave 3,21-diacetoxy-17-hydroxy-1-methyl-19-nor-9β-pregna-1,3,5(10)-triene-11,20-dione (0·16 g., 35%), m. p. 187—189°, $[\alpha]_D$ +121°.

Degradation of **3,21-*Diacetoxy*-17-*hydroxy*-1-*methyl*-19-*nor*-9β-*pregna*-1,3,5(10)-*triene*-11,20-*dione*.**—The steroid (1·81 g.) in tetrahydrofuran (75 ml.) was reduced with lithium aluminium hydride (2·0 g.) in tetrahydrofuran (75 ml.) as described above for the 9α-compound. The crude product (1·49 g.) was methylated as above and the crude monomethyl ether (1·43 g.) was treated with sodium metaperiodate (2·1 g.), to give a mixture containing the epimeric 11-hydroxy-3-methoxy-1-methyl-9β-œstra-1,3,5(10)-trien-17-ones (XI) (1·098 g.). This material, in 1 : 1 hexane–benzene, was chromatographed on alumina (30 g.). The steroids were eluted, without apparent fractionation, by benzene, benzene–ether, and ether. Paper chromatography showed two spots in all the eluates, the slower-running spot becoming relatively more intense in the later fractions. The fractions were combined (0·752 g.), dissolved in chloroform (12 ml.) containing pyridine (2·4 ml.), and treated with methanesulphonyl chloride (1·5 ml.). The mixed methanesulphonates were treated with sodium acetate (2·4 g.) and acetic acid (24 ml.) as described above, and the product (660 mg.) was chromatographed on alumina (grade I; 20 g.). Hexane containing 20% and then 50% of benzene eluted 3-methoxy-1-methylœstra-1,3,5(10), 9(11)-tetraen-17-one which, after crystallisation from aqueous methanol, weighed 301 mg. (25%) and melted at 95—97°; there was no depression of m. p. on admixture with material prepared as described above, and the infrared spectra were identical.

Equilibration of **3,21-*Diacetoxy*-17-*hydroxy*-1-*methyl*-19-*norpregna*-1,3,5(10)-*triene*-11,20-*dione and its* 9β-*Epimer*.**—Treatment of the 9α-epimer with a 5% solution of perchloric acid in acetic acid at room temperature resulted in a change of specific rotation from +253° to +162° in *ca.* 56 hr. Under the same conditions, the rotation of the 9β-epimer changed from +116° to +162° in about 16 hr. Reacetylation of the product from the 9α-epimer with acetic anhydride and pyridine gave a mixture whose infrared spectrum was consistent with its containing both epimers; again, paper chromatography of each product suggested that they were similar mixtures of the 9-epimers.

The 9α-epimer (0·5 g.) in acetic acid (75 ml.) was treated with aqueous 60% w/w perchloric

acid (3·75 ml.). After 26 hr. the specific rotation was constant at +163°. After a further 16 hr. the solution was poured into water, and the product was isolated with ethyl acetate and treated overnight at room temperature with acetic anhydride (5 ml.) and pyridine (5 ml.). The product (0·5 g.) had $[\alpha]_D$ +132°. This material (0·42 g.) was chromatographed on Florisil (25 g.). Benzene containing 10—15% of ethyl acetate eluted 0·205 g. of material with m. p. varying from 182° to 220°, and infrared spectra suggestive of 9β-epimer contaminated with some of the 9α-compound. Crystallisation from ethanol gave a first crop of prisms (28 mg.), m. p. 225—233°, $[\alpha]_D$ +269° (*c* 0·9), consisting substantially of the 9α-compound. A second crop consisted of a mixture of prisms and rosettes, which could be largely separated by virtue of their different densities. The prisms (10·5 mg.), m. p. 230—239°, $[\alpha]_D$ +267° (*c* 0·66), again consisted of the 9α-epimer. The needles (62 mg.), m. p. 185—206°, $[\alpha]_D$ +162° (*c* 0·9), appeared to consist chiefly of the 9β-epimer, but an attempt to purify them further by crystallisation was unsuccessful.

3-*Acetoxy*-1-*methylœstra*-1,3,5(10)-*triene*-11,17-*dione* (XIII; R = Ac).—Androsta-1,4-diene-3,11,17-trione [5] (10 g.) in acetic anhydride (280 ml.) was shaken with a mixture of 60% w/w aqueous perchloric acid (0·3 ml.) and acetic anhydride (20 ml.) for 6 hr. at room temperature and poured into aqueous sodium hydrogen carbonate. Isolation with ethyl acetate gave material with $\lambda_{max.}$ 235 mμ ($E^{1\%}_{1\,cm.}$ 86). Chromatography on Florisil (100 g.) gave, in the fractions eluted with benzene and 1 : 1 benzene–ethyl acetate, 3-*acetoxy*-1-*methylœstra*-1,3,5(10)-*triene*-11,17-*dione* (7·8 g., 69%), m. p. 203—208°, $[\alpha]_D$ +375° (*c* 1·0) (Found: C, 74·3; H, 7·3. $C_{21}H_{24}O_4$ requires C, 74·1; H, 7·1%), $\nu_{max.}$ (in Nujol) 1740 (OAc and 17-C=O), 1710 (11-C=O), 1220 (OAc), and 845 cm.$^{-1}$ (*meta*-type).

3-*Hydroxy*-1-*methylœstra*-1,3,5(10)-*triene*-11,17-*dione* (XIII; R = H).—The foregoing 3-acetoxy-compound (4 g.) in methanol (300 ml.) was treated with potassium hydroxide (1 g.) in methanol (20 ml.) under nitrogen and the solution was stirred at room temperature for 1 hr. Acetic acid was added to neutralise the alkali, followed by water, and the methanol was evaporated under reduced pressure. On being left overnight at 0°, the solution deposited 3-*hydroxy*-1-*methylœstra*-1,3,5(10)-*triene*-11,17-*dione* (2·54 g., 72%), m. p. 230—233° (from methanol), $[\alpha]_D$ +426° (*c* 1·0 in acetone) (Found: C, 76·5; H, 7·4. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·4%), $\nu_{max.}$ (in $CHBr_3$) 3600 (OH), 1742 (17-C=O), 1716 (11-C=O), and 844 cm.$^{-1}$ (*meta*-type).

This material (70 mg.) with pyridine (1 ml.) and acetic anhydride (1 ml.) overnight at room temperature gave the 3-acetoxy-compound, m. p. 203—205°, $[\alpha]_D$ +375° (*c* 1·0), identical with material prepared as described above.

Epimerisation of 3-*Acetoxy*-1-*methylœstra*-1,3,5(10)-*triene*-11,17-*dione*.—The steroid (500 mg.) in acetic acid (50 ml.) was treated with 60% perchloric acid (2·5 ml.) and left under nitrogen, in the dark, for 6 days. Addition to water gave a clear solution, which was extracted with ether (3 × 300 ml.). The extract was washed with aqueous sodium hydrogen carbonate and water. The extracts were dried ($MgSO_4$) and evaporated, to give a blue semi-solid residue (474 mg.), whose infrared spectrum showed that the acetate group had been hydrolysed. Trituration with a little ether gave a solid (342 mg.), which was extracted with boiling ether to leave a residue (62 mg.) of 3-hydroxy-1-methylœstra-1,3,5(10)-triene-11,17-dione, m. p. 226—231°. The ether extracts, on evaporation to small bulk and storage at 0°, gave a solid (158 mg.), m. p. 200—212° (decomp.). Crystallisation from a little methanol gave 46 mg. of a substance, probably essentially 3-*hydroxy*-1-*methyl*-9β-*œstra*-1,3,5(10)-*triene*-11,17-*dione* (XIV), m. p. 195—205° (decomp.), $[\alpha]_D$ +242° (*c* 0·81 in acetone) (Found: C, 75·6; H, 7·6. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·4%), $\nu_{max.}$ (in $CHBr_3$) 1736 (17-C=O), 1710 (11-C=O), and 842 cm.$^{-1}$ (*meta*-type).

Comparative Rates of Aromatisation of Prednisone Acetate, Prednisolone Acetate, and Cholesta-1,4-*dien*-3-*one*.—Prednisone acetate (0·4 g.), prednisolone acetate (0·4 g.), and cholesta-1,4-dien-3-one (0·38 g.) were separately added to alcohol-free chloroform (10 ml.) and the mixtures were each treated with 2·5 ml. of a 0·125% solution of perchloric acid in acetic anhydride. The prednisolone acetate went into solution only after shaking for ½ hr.; the others dissolved at the outset. At intervals, 1 ml. samples were withdrawn, added to ice and extracted with chloroform. The extracts were washed with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated. The ultraviolet spectra of the residues were examined, with the results shown in the Table.

Aromatisation of Prednisolone Acetate.—Prednisolone acetate (5 g.), suspended in chloroform (alcohol-free; 80 ml.), was treated with a solution prepared by the addition, at 0°, of 60% w/w aqueous perchloric acid (0·025 ml.) to acetic anhydride (20 ml.), and the mixture was shaken

XUM

Time (hr.)	Prednisone acetate $\lambda_{max.}$	Prednisone acetate $E^{1\%}_{1\,cm.}$	Prednisolone acetate $\lambda_{max.}$	Prednisolone acetate $E^{1\%}_{1\,cm.}$	Cholesta-1,4-dien-3-one $\lambda_{max.}$	Cholesta-1,4-dien-3-one $E^{1\%}_{1\,cm.}$
0	238	362	242	378	244	431
1	237	350	242 *	64	243 *	14·4
2·5	237	325	242 *	55	243 *	12
6	236·5	241	242 *	38·4		
24	237	246	242 *	22·9		

* No maximum.

for 3 hr.; after 1 hr. the prednisolone acetate was in solution. Aqueous sodium hydrogen carbonate was added, and the chloroform layer was separated, washed with further sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated to dryness under reduced pressure. The crude product, whose spectra indicated the presence of about 20% of unchanged prednisolone acetate, was chromatographed on Florisil (100 g.). Hexane–benzene gave a product (0·1 g.), probably substantially 1,11β,17,21-tetra-acetoxy-4-methyl-19-norpregna-1,3,5(10)-trien-20-one (XXI; $R^1 = R^2 = Ac$); $\nu_{max.}$ (in $CHBr_3$) 1745—1735 and 1240—1210 (OAc), and 812 cm.$^{-1}$ (*para*-type) (no hydroxyl bands). Benzene, and benzene containing ethyl acetate, gave material that appeared, from infrared spectra and paper chromatography, to consist chiefly of a triacetate, presumably the 1,17,21-triacetate (XXI; $R^1 = Ac$, $R^2 = H$), $\nu_{max.}$ (in $CHBr_3$) 3580 (OH), 1750 and 1215 (aromatic OAc), 1730 and 1245 (OAc), and 812 cm.$^{-1}$ (*para*-type). This could not be obtained crystalline.

The crude product (4·8 g.), obtained by aromatisation of prednisolone acetate (5·0 g.) as described above and removal of unchanged $\Delta^{1,4}$-3-ketone by chromatography on Florisil, was dissolved in methanol (150 ml.), and 1·4N-methanolic sodium methoxide (23·2 ml.) was added under nitrogen. After 4 min. water (0·6 ml.) was added followed, after a further 5 min., by water (60 ml.) and acetic acid (9 ml.). The methanol was distilled off under reduced pressure and the residue was diluted with water and left overnight at 0°. The resulting white solid (2·5 g.) appeared from paper chromatography to contain two compounds. Crystallisation from aqueous methanol gave 11β-*acetoxy*-1,17,21-*trihydroxy*-4-*methyl*-19-*norpregna*-1,3,5(10)-*trien*-20-*one* (XXI; $R^1 = H$, $R^2 = Ac$) (1·2 g., 24%), m. p. 218—222°. Recrystallisation from aqueous methanol gave material with m. p. 225—227°, $[\alpha]_D$ +175° (*c* 1·0 in acetone), which ran as a single spot on paper (Found: C, 68·1; H, 7·5. $C_{23}H_{30}O_6$ requires C, 68·6; H, 7·5%), $\nu_{max.}$ (in Nujol) 3530 and 3300 (OH), 1730 and 1248 (OAc), 1710 (C=O) and 805 cm.$^{-1}$ (*para*-type).

Degradation of the Aromatisation Product of Prednisolone Acetate.—Material (3·24 g.), obtained as above by aromatisation of prednisolone acetate and removal of $\Delta^{1,4}$-3-ketone and coloured impurities by chromatography on Florisil, was added in tetrahydrofuran (100 ml.) to a stirred solution of lithium aluminium hydride (3 g.) in tetrahydrofuran (100 ml.). The mixture was boiled under reflux under nitrogen, with stirring, for 4 hr. and then left overnight at room temperature. After addition of ethyl acetate and water, 2N-sulphuric acid was added, and the product was isolated with ethyl acetate to give a crude material (2·06 g.), whose infrared spectrum showed the presence of some unreduced ketone. This material, in methanol (100 ml.), was methylated with dimethyl sulphate and alkali as described above. Isolation with ethyl acetate gave the crude monomethyl ether, which was dissolved in ethanol (140 ml.) and water (210 ml.) and treated with sodium metaperiodate (2·8 g.). After 24 hr. at room temperature the mixture was diluted with water, and the product (1·42 g.) was isolated with ether. Chromatography on acid-washed alumina (grade I; 50 g.) gave, first, materials whose infrared spectra showed them to be deficient in hydroxyl. Benzene–ether (1 : 1) eluted material, which, on trituration with a little ether, gave a solid (240 mg.), m. p. 83—87°. Crystallisation from aqueous methanol gave the supposed 11β-*hydroxy*-1-*methoxy*-4-*methylœstra*-1,3,5(10)-*trien*-17-*one* (XXII) as long needles, m. p. 86—87°, $[\alpha]_D$ +80·8° (*c* 0·9) (Found: C, 76·6; H, 9·1. $C_{20}H_{28}O_3$ requires C, 76·4; H, 8·3%), $\nu_{max.}$ (in CS_2) 3620 (OH), 1740 (17-C=O), 1254 and 1046 (OMe), and 812 and 798 cm.$^{-1}$.

The authors are indebted to Dr. J. E. Page for interpreting the infrared spectra.

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX. [*Received, February 23rd,* 1961.]

894. *Compounds related to the Steroid Hormones. Part V.* The Partial Synthesis of 21-Acetoxy-17-hydroxy-16β-methyl-5α-pregn-9-ene-3,20-dione.*

By J. Attenburrow, J. E. Connett, W. Graham, J. F. Oughton, A. C. Ritchie, and P. A. Wilkinson.

A ten-stage process is described for the conversion of 3β-acetoxy-5α-pregna-9,16-dien-20-one into 21-acetoxy-17-hydroxy-16β-methyl-5α-pregn-9-ene-3,20-dione. The 9(11)-unsaturated bond was protected during formation of the dihydroxyacetone side chain by use of 9α,11β-dichloro-intermediates. Isolation and characterisation of the 20-enol form of 3β-acetoxy-16β-methyl-5α-pregn-9(11)-en-20-one is described.

16α- and 16β-Methyl corticoids having greater gluco-corticoid activity than the non-methylated parents have been obtained in the past from bile acid intermediates [1] and from diosgenins.[2] This paper describes a route, with alternatives, shown in the accompanying flowsheet, to a useful † 16β-methylcorticoid precursor (XVIII), from 3β-acetoxy-5α-pregna-9,16-dien-20-one (I), which in turn may be obtained readily from hecogenin.[3]

Introduction of the methyl group in the 16-position by way of the 16,17-pyrazoline [4] presented little difficulty, and the 3β-acetoxy-16-methyl-5α-pregna-9,16-dien-20-one (III) was obtained in about 68% overall yield. Pyrolysis of 16,17-pyrazolines has been done in the past [1d,4,5] by melting the compound under reduced pressure, but we preferred to use a liquid medium for greater temperature control: diethylene glycol was found convenient, as the product could be isolated by dilution with water.

For the introduction of the 17α-hydroxyl group two routes were available. The first involved the Julian procedure [6] with selective epoxidation at the 16,17-position by means of alkaline peroxide, treatment with hydrogen bromide, and hydrogenation. The second route entailed selective hydrogenation at the 16,17-position and the Gallagher procedure.[7] As the latter route was likely to be complicated by the need either to carry out two selective reactions or to introduce protective groups, the former was examined first but the product obtained was not homogeneous and consisted largely of the 16α-methyl compound.‡ We therefore turned to the second line of approach.

Under basic conditions, with palladium–charcoal as catalyst, the 16-methyl-9,16-diene (III) was hydrogenated at the 16-position, leaving the 9(11)-position almost unattacked (>97% shown present by peracid titration and by infrared absorption at 820 cm.$^{-1}$), to

* Part IV, preceding paper.

† See Part VI, succeeding paper.

‡ Wendler and his co-workers [1f] recently reported that the perchloric acid-rearranged product from 16α,17α-epoxy-3α-hydroxy-16β-methylpregnane-11,20-dione gave, on hydrogenation in the presence of palladium–calcium carbonate, a 7 : 3 mixture of the 3α,17α-dihydroxy-16α- and -16β-methylpregnane-11,20-diones.

[1] (*a*) Arth, Johnston, Fried, Spooncer, Hoff, and Sarett, *J. Amer. Chem. Soc.*, 1958, **80**, 3160; (*b*) Arth, Fried, Johnston, Hoff, Sarett, Silber, Stoerk, and Winter, *ibid.*, p. 3161; (*c*) Oliveto, Rausser, Nussbaum, Gebert, Herschberg, Tolksdorf, Eisler, Perlman, and Pechet, *ibid.*, p. 4428; (*d*) Taub, Hoffsommer, Slates, and Wendler, *ibid.*, p. 4435; (*e*) Oliveto, Rausser, Herzog, Herschberg, Tolksdorf, Eisler, Perlman, and Pechet, *ibid.*, p. 6687; (*f*) Karady and Sletzinger, *Chem. and Ind.*, 1959, 1159; (*g*) Wendler and Taub, *ibid.*, 1958, 415; (*h*) Hoffsommer, *J. Org. Chem.*, 1959, **24**, 1617; (*i*) Taub, Hoffsommer, Slates, Kuo, and Wendler, *J. Amer. Chem. Soc.*, 1960, **82**, 4012.

[2] Oliveto, Rausser, Weber, Nussbaum, Gebert, Coniglio, Herschberg, Tolksdorf, Eisler, Perlman, and Pechet, *J. Amer. Chem. Soc.*, 1958, **80**, 4431.

[3] Djerassi, Martinez, and Rosenkranz, *J. Org. Chem.*, 1951, **16**, 1278; Callow and James, *J.*, 1956, 4739.

[4] Wettstein, *Helv. Chim. Acta*, 1944, **27**, 1803.

[5] Bernstein and Joseph, *J. Org. Chem.*, 1960, **25**, 1676.

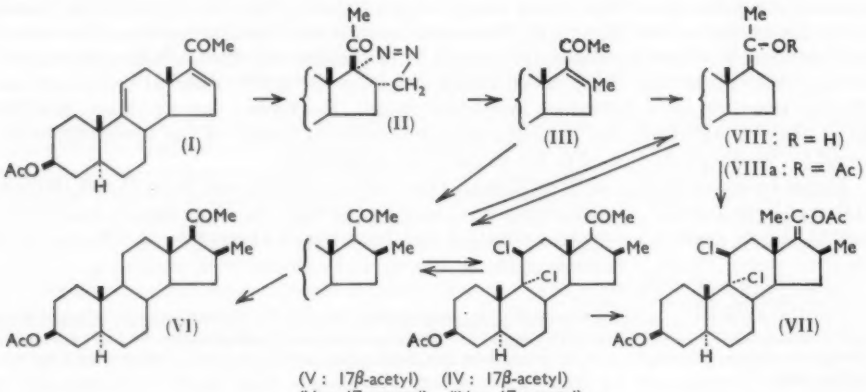
[6] Julian, Meyer, Karpel, and Waller, *J. Amer. Chem. Soc.*, 1950, **72**, 5145.

[7] Kritchevsky, Garmaise, and Gallagher, *J. Amer. Chem. Soc.*, 1952, **74**, 483.

XUM

give, as expected on theoretical grounds (see also refs. 1*c*, 1*d*), the 16β-methyl compound (V). The structure of this compound was established by further hydrogenation, this time under acid conditions on palladium–charcoal, to a product whose physical constants agreed well with those described [8] for 3β-acetoxy-16β-methyl-5α-pregnan-20-one (VI).

During the experimental work in this field it was found that hydrogenation of the 16-methyl-diene (III) at room temperature as a dilute solution in a mixture of tetrahydrofuran and triethylamine led, provided that low temperatures were used in the subsequent evaporation, to a product less soluble in acetone than the normal hydrogenation product. The less soluble fraction (28%) melted some 30° the higher and its infrared spectrum in Nujol showed the presence of a hydroxyl group, with no evidence for 20-carbonyl absorption. A 17-en-20-ol structure was ascribed to this new compound for the reasons given below. Its analyses were correct for $C_{24}H_{36}O_3$ and showed an active hydrogen content of 0·21% (calc. 0·27%), whereas the ketone contained no active hydrogen. In carbon disulphide the infrared spectrum indicated a gradual change from the enol to the keto-form. The enol (VIII) changed at 100° (*in vacuo*) into a mixture of the 17α- and 17β-acetyl compounds, as shown by a drop in rotation and by infrared evidence: this heat-sensitivity could account for the indefinite melting point. The rotation of the enol in dioxan appeared to be slightly higher than that of the 17β-acetyl compound but accurate determination of this constant was impossible owing to the rearrangement that occurred in solution; for example, keeping a solution of the enol in tetrahydrofuran for 30 minutes and recovery by evaporation in the cold gave a product of decreased enol content (as estimated by infrared evidence); and if a similar solution was stirred for 30 minutes with twice its weight of active carbon, all trace of enol disappeared and only the 17β-material (V) could be recovered. No ferric chloride colour has been obtained with the enol.



Unlike the corresponding ketone, the enol was acetylated at room temperature in a mixture of acetic anhydride and pyridine, giving a diacetate (VIIIa), but also some of the 20-ketone (V), presumably arising from isomerisation of the enol before acetylation. Enols are known [9] to absorb oxygen readily in neutral solution, with the formation of hydroperoxides, and this compound (VIII) in benzene absorbed 1·75 mol., to give products of undetermined structure; when the oxygen uptake was restricted to 1 mol. the 17-hydroperoxide was isolated. Neither the 16β-methyl-20-ketone (V) nor the corresponding

[8] Romo, Lepe, and Romero, *Bol. Inst. Quím. Univ. nac. auton. México* IV, 1952, 125.
[9] Criegee, "Methoden der organischen Chemie," Georg Thieme Verlag, Stuttgart, 4th edn., Vol. VIII, p. 25.

17,20-enol acetate (VIIIa) absorbed oxygen under these conditions, which is not surprising, since it has been recently shown [10] that for 17-hydroperoxidation of steroidal 20-ketones it is necessary to form the anion of the ketone by means of potassium t-butoxide.

In tetrahydrofuran solution the introduction of dilute hydrochloric acid to bring the concentration to 0·001N converted the enol (VIII), presumably under kinetic control, into the thermodynamically unstable [4,8] β-side-chain ketone, whereas the same concentration of sodium hydroxide produced a mixture of α- and β-side-chain ketones, as shown by an almost instantaneous drop in the optical rotation of the solution. The change from enol to ketone in these solutions was confirmed by infrared examination.

Hydrogenation of conjugated ketones to enols by 1,4-addition has been discussed in the literature.[11] Presumably hydrogenation of the Δ^{16}-20-ketone (III) must occur mainly, if not completely, by this mechanism, for yields as high as 28% of the enol have been isolated despite its ready isomerisation to the ketone in solution, particularly in the presence of charcoal.

Recently, the enol of a steroid 20-ketone has been isolated [12] as a by-product of 16,17-hydrogenation of a Δ^{16}-20-oxo-21-ester in the aldosterone series. The stability of the enol isolated by the Swiss workers might be explained by hydrogen bonding between the 20-hydroxyl group and the oxygen of the 21-ester group, whereas the stability of our enol is presumably due to steric factors associated with the presence of a 16β-methyl group.

As one of the steps in the Gallagher process for the introduction of the 17α-hydroxyl group involves epoxidation of the 17,20-double bond by peracid, clearly an unprotected 9,11-double bond would also be prone to attack. To avoid this we studied the 9α,11β-dichloro-derivatives,[13] which are readily formed, reasonably stable, and yet easily converted into the parent unsaturated compounds by chromous chloride reduction. The method of preparation preferred by the American authors [13] involved the use of hydrogen chloride, which might, however, invoke in our compound undesirable chlorine substitution at $C_{(17)}$ or $C_{(21)}$, and therefore their second method of direct addition, with a solution of chlorine in an organic solvent, was investigated.

Reaction of 3β-acetoxy-16β-methyl-5α-pregn-9(11)-en-20-one (V) in carbon tetrachloride by the addition of 1·1 mol. of chlorine in the same solvent took place readily, but the product was grossly impure, and a yield of only 40% of the desired 9α,11β-dichloro-compound was obtained. Reduction of the crude product by chromous chloride gave a monochloro-compound with a specific rotation of +120°, indicating that chlorination had occurred at other reactive centres, for example, at $C_{(17)}$.

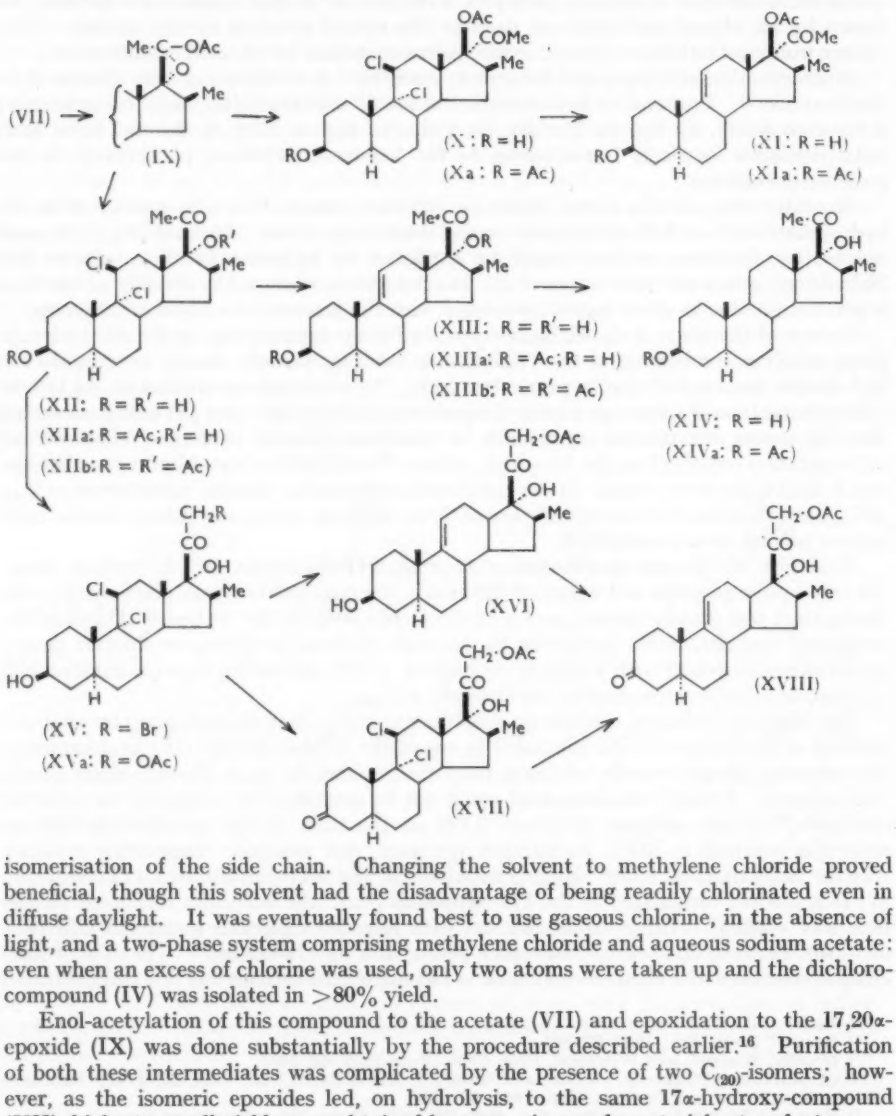
The effect of hydrogen chloride on substituents at $C_{(17)}$ was demonstrated by adding a solution of hydrogen chloride in ethanol to one of the dichloro-ketone (IV) in chloroform: the rotation changed rapidly at room temperature, and the pure 17α-side-chain isomer was isolated. Though this compound could not be identified by comparing its recorded constants,[14] it was assigned structure (IVa) on the basis of the considerable drop in molecular rotation (−238°), its infrared spectrum, and analysis. Supporting evidence was the isomerisation, under similar conditions, of the 9(11)-unsaturated 17β-compound (V) to a product formulated as the 17α-compound (Va); the molecular rotational change here was −279·5°. These values contrast with recorded molecular rotational difference of −540° between 3β-acetoxy-5α-pregnan-20-one and its 17α-isomer.[15] The ease of side-chain isomerism under alkaline conditions in 16β-methyl-20-ketones was first demonstrated

[10] Bailey, Elks, and Barton, *Proc. Chem. Soc.*, 1960, 214.
[11] Burwell, *Chem. Rev.*, 1957, **57**, 895.
[12] Heusler, Wieland, and Wettstein, *Helv. Chim. Acta*, 1959, **42**, 1586.
[13] Cf. Robinson, Finckenor, Oliveto, and Gould, *J. Amer. Chem. Soc.*, 1959, **81**, 2191; Reimann, Oliveto, Neri, Eisler, and Perlman, *ibid.*, 1960, **82**, 2308.
[14] Ryer and Gebert, *J. Amer. Chem. Soc.*, 1952, **74**, 4336; Romo, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1951, **73**, 4961; Barton and Cox, *J.*, 1948, 783.
[15] Shoppee, *J.*, 1949, 1671.

XUM

by Wettstein.[4] Romo, Lepe, and Romero [8] later found that 3β-acetoxy-16β-methylpregn-5-en-20-one gave the 17α-isomer under both acid and alkaline conditions: the latter was reduced to the saturated 17α-isomer of (VI). The $\Delta[M]_D$ in this case was −346°, which is more in keeping with our findings.

An attempt to remove hydrogen chloride from the carbon tetrachloride solution of chlorine with solid sodium hydrogen carbonate did not improve the reaction; nor did introduction of organic bases—presumably base hydrochlorides are equally effective in



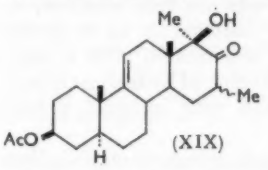
isomerisation of the side chain. Changing the solvent to methylene chloride proved beneficial, though this solvent had the disadvantage of being readily chlorinated even in diffuse daylight. It was eventually found best to use gaseous chlorine, in the absence of light, and a two-phase system comprising methylene chloride and aqueous sodium acetate: even when an excess of chlorine was used, only two atoms were taken up and the dichloro-compound (IV) was isolated in >80% yield.

Enol-acetylation of this compound to the acetate (VII) and epoxidation to the 17,20α-epoxide (IX) was done substantially by the procedure described earlier.[16] Purification of both these intermediates was complicated by the presence of two $C_{(20)}$-isomers; however, as the isomeric epoxides led, on hydrolysis, to the same 17α-hydroxy-compound (XII), highest overall yields were obtained by processing crude materials at each stage.

[16] Barton, Evans, Hamlet, Jones, and Walker, *J.*, 1954, 747.

The alternative route to the dichloro-enol acetate (VII) through the enol acetate (VIIIa) was investigated with the aim of avoiding formation of 17-chloro-compounds, but the yield of 9,11-dichloro-compound was low.

Owing to the instability of 9,11-dichloro-compounds in hot methanol, the usual method of hydrolysis of 3,20-diacetoxy-17,20-epoxides to 3,17-diols with hot methanolic alkali [16] was avoided, and hydrolysis under acid conditions was explored instead. Acetic acid containing a small quantity of aqueous sulphuric acid gave the dichloro-3β-acetoxy-17α-hydroxy-compound (XIIa), which, being more soluble than the corresponding 3,17-diol (XII), was readily purified. Dechlorination, by chromous chloride or, better, by hydrogenolysis under basic conditions with palladised charcoal, gave the 9,11-unsaturated compound (XIIIa), which was hydrogenated under acidic conditions to 3β-acetoxy-17-hydroxy-16β-methyl-5α-pregnan-20-one (XIVa). The 3-hydroxy-compound (XIV) was obtained by methanolysis at room temperature with aqueous sulphuric acid as catalyst.



(XIX)

The unsaturated diol (XIII) was obtained satisfactorily by cold acid methanolysis of the 3-acetate (XIIIa) whereas hot acid led to a product that, after acetylation, had a low rotation and an infrared spectrum typical of a D-homo-steroid. This compound, on the basis of the usual type of D-homo-rearrangement, is provisionally formulated as (XIX).

Unlike what occurs in the preparation [17] of 21-bromo-3β,17-dihydroxy-5α-pregn-9(11)-en-20-one, bromination of our 9,11-unsaturated diol (XIII) by the same method produced an unstable product containing 50% of 9,11-dibromides, as shown by reduction in the height of the Δ^9-band at 820 cm.$^{-1}$ and the continuous release of hydrogen bromide.

It thus became evident that protection of the 9,11-position by chlorine should be continued during the introduction of the 21-acetate group. First, however, a suitable medium for hydrolysis of the diacetate (IX) to the diol (XII) had to be found, particularly in view of the instability of the dichloro-compound to hot methanol and the insolubility of both (IX) and (XII) in most solvents.

Hydrolysis in methanol–methylene chloride–aqueous sulphuric acid gave the required diol in reasonable yield, but from the mother-liquors an unexpected new compound, formulated as 17β-acetoxy-9α,11β-dichloro-3β-hydroxy-16β-methyl-5α,17α-pregnan-20-one (X), was isolated in 10—15% yield. The structure assigned to this compound was based on its ultimate analysis and on infrared examination, which indicated the presence of a 9α,11β-dichloro-structure, an acetyl group, and one hydroxyl group, the latter not being in the 17-position (absorption at 1720 cm.$^{-1}$ of a non-hydrogen-bonded ketone). Acetylation of this compound produced a diacetate (Xa) with the same analysis as the diacetate (XIIb) but differing from the latter in crystalline form, optical rotation, melting point, and infrared spectrum, which for each compound showed the presence of normal non-hydrogen-bonded ketone and the absence of enol acetate structure. Hydrogenolysis of compounds (Xa) and (XIIb) gave different $\Delta^{9(11)}$-diacetates (XIa and XIIIb), indicating that the isomerism was not associated with the disposition of the chlorine atoms.

Rearrangements similar to (IX ⟶ Xa) have been reported [18] from heating 17,20-epoxide 20-acetates above their melting points or allowing them to stand in light petroleum over silica gel. Heating our epoxide (IX) to 20° above its melting point for 10 minutes gave a crude product from which the 17β-acetate (Xa) was obtained in 15% yield. The structure of the latter is further supported by its conversion [19] by zinc dust in acetic acid into 3β-acetoxy-16β-methyl-5α-pregn-9(11)-en-20-one (V).

Reducing the quantity of water in the hydrolysis medium largely avoided the formation of the 17β-acetoxy-impurity, but much better results were obtained by methanolysis at

[17] Elks, Phillipps, and Wall, *J.*, 1958, 4001.
[18] Soloway, Considine, Fukushima, and Gallagher, *J. Amer. Chem. Soc.*, 1954, **76**, 2941.
[19] Rosenfeld, *J. Amer. Chem. Soc.*, 1957, **79**, 5540.

XUM

room temperature under alkaline conditions with sufficient methylene chloride to dissolve the epoxide (IX).

In the bromination of the dichloro-diol (XII) to the 21-bromide (XV) the general method of Pataki, Rosenkranz, and Djerassi [20] with our modifications [21] for the 21-bromination of 3β,17α-dihydroxy-5α-pregnane-11,20-dione was employed. The 21-bromide was converted in good yield into the 21-acetate (XVa) by potassium acetate in refluxing acetone, provided the time of reaction was strictly limited: longer times led to dehydrochlorination, with the formation of a 7,9(11)-diene system, as shown by appearance of the ultraviolet maximum at 242 mμ. However, the 16β-methyl-21-acetate (XVa) could not be freed from unchanged dichloro-diol (XII) by the method that we [22] have previously used for 11-keto-21-acetates unsubstituted in the 16-position. Presumably the 16β-group hinders the approach of the Girard reagent to the 20-ketone in the parent 21-methyl compound. As removal of this impurity by recrystallisation was not very effective, we modified the bromination conditions and the procedure for isolation so as to obtain substantially pure 21-bromide (XV): the suspended steroid was treated with a slight excess of bromine in chloroform containing 8% of ethanol and 10 mol. of hydrogen chloride and the steroid–hydrogen chloride complex was decomposed with aqueous sodium hydrogen carbonate.

The 9,11-unsaturation was reintroduced, in good yield, by hydrogenolysis on palladium or reduction with chromous chloride or zinc dust, but oxidation of the 3-hydroxyl group in the unsaturated compound (XVI) by the standard procedure [23] (potassium dichromate–sulphuric acid in acetone) led to substantial degradation of the steroid. The 3-hydroxyl group of the dichloro-compound (XVa) was therefore oxidised, before removal of the protective chlorine atoms, with chlorine in acetic acid in the presence of a buffer. This procedure has been described [24] for selective oxidation in the 20-position of 5,6-dichloropregnane-3,20-diols, but this appears to be its first use for preparation of a 3-ketone from a 3-hydroxy-compound. Finally, 9,11-unsaturation was reintroduced, as before, by hydrogenolysis or by zinc dust and acetic acid, the latter giving a yield of 93% over both stages.

Experimental

M. p.s were determined with capillary tubes in an electrically heated block and are corrected. Optical rotations refer to *ca.* 1% chloroform solutions at 20°. Infrared spectra are for solutions in CS_2 unless otherwise stated, determined with a Perkin–Elmer model 21 double-beam spectrophotometer equipped with rock-salt optics.

3β-*Acetoxy*-16β(H)-1′-*pyrazolino*(4′,3′:16,17)-5α-*pregn*-9-*en*-20-*one* (II).—*N*-Nitrosomethylurea (80 g.) was added to a solution of 3β-acetoxy-5α-pregna-9,16-dien-20-one (104 g.) in methylene chloride (1·0 l.). A 50% aqueous solution (160 ml.) of potassium hydroxide was added at −5° during 30 min. and the reaction allowed to become complete at room temperature during 2 hr. Water (1·5 l.) was added slowly and the mixture was stirred for 15 min. in order to discharge any excess of diazomethane. The layers were separated; the aqueous phase was extracted with methylene chloride (1 × 300 ml.), and the organic phase washed with water (3 × 350 ml.), the methylene chloride extract being used as a back-wash. The residue obtained by distillation of the combined methylene chloride solutions was triturated with light petroleum (750 ml.; b. p. 100—120°). The resulting solid was dried *in vacuo* at 100° to give the *pyrazoline* (106·5 g., 92%), m. p. 158° (decomp.), $[\alpha]_D$ +72°, $\lambda_{max.}$ 229 mμ (ε 1167) (Found: C, 72·2; H, 8·9; N, 6·9. $C_{24}H_{34}N_2O_3$ requires C, 72·4; H, 8·6; N, 7·0%).

3β-*Acetoxy*-16-*methyl*-5α-*pregna*-9,16-*dien*-20-*one* (III).—The pyrazoline (II) (222 g.) was added portionwise in 25 min. with stirring to diethylene glycol (880 ml.) at 165°. When nitrogen evolution had stopped at this temperature the mixture was cooled to 100° and water (3·0 l.)

[20] Pataki, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 5615.
[21] B.P. 761,009.
[22] B.P. 762,716.
[23] Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402.
[24] U.S.P. 2,811,522.

added. The crude product crystallised from ethanol to yield 3β-*acetoxy*-16-*methyl*-5α-*pregna*-9,16-*dien*-20-*one* (146 g., 71%), m. p. 139—142°, $[\alpha]_D$ +53°, $\lambda_{max.}$ 249 mμ (ε 8595), $\nu_{max.}$ 1735 and 1240 (OAc), 1658 (CO·C=C), and 820 cm.$^{-1}$ (9-C=C) (Found: C, 77·6; H, 9·3. $C_{24}H_{34}O_3$ requires C, 77·8; H, 9·2%).

3β-*Acetoxy*-16β-*methyl*-5α-*pregn*-9-*en*-20-*one* (V).—(a) *From* 3β-*acetoxy*-16-*methyl*-5α-*pregna*-9,16-*dien*-20-*one* (III). The diene (2·0 kg.) in tetrahydrofuran (12 l.) and triethylamine (2·0 l.) was hydrogenated at atmospheric pressure over 10% palladium oxide on charcoal (170 g.). When the hydrogen uptake ceased (139·8 l. in 150 min.) the catalyst and solvent were removed. The residue crystallised from methanol to give a product (1999 g.), m. p. 106—110°, $[\alpha]_D$ +30·2°. This generally contained *ca.* 3% of 9,11-saturated compound (estimated by the 820 cm.$^{-1}$ maximum and by peracid titration) which it was impossible to remove by crystallisation at this stage. The pure product was obtained by dechlorination of the corresponding 9α,11β-dichloro-compound as described in experiment (b).

(b) *From* 3β-*acetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α-*pregnan*-20-*one* (IV). The dichloro-ketone (50 g.) in acetone (1·0 l.) and water (100 ml.) under a rigorously maintained atmosphere of carbon dioxide was treated with 2·3N-chromous chloride (300 ml.) at room temperature for 30 min. The product, isolated by dilution with water, recrystallised from methanol as plates (31·3 g., 74·5%), m. p. 113—115°, $[\alpha]_D$ +34·2°. A sample, recrystallised from methanol, gave 3β-*acetoxy*-16β-*methyl*-5α-*pregn*-9-*en*-20-*one*, m. p. 114—115°, $[\alpha]_D$ +32·7° (Found: C, 77·4; H, 9·75. $C_{24}H_{36}O_3$ requires C, 77·4; H, 9·75%), $\nu_{max.}$ 1735 and 1245 (OAc), 1708 (C=O) and 822 cm.$^{-1}$ (9-C=C) (Δ^9-bond 99·3% by peracid titration).

3β-*Acetoxy*-16β-*methyl*-5α-*pregnan*-20-*one* (VI).—3β-Acetoxy-16β-methyl-5α-pregn-9-en-20-one (V) (1·3 g.) in acetic acid (52 ml.) was hydrogenated over pre-reduced 10% palladium–charcoal (0·92 g.). Hydrogen uptake (~1 mol.) was complete in 1½ hr. Removal of the catalyst, concentration of the filtrate under reduced pressure, and precipitation of the product with water gave 3β-acetoxy-16β-methyl-5α-pregnan-20-one (1·33 g.), m. p. 148—151°, $[\alpha]_D$ +30° (cf. ref. 8 which gives m. p. 148°, $[\alpha]_D$ +29·5°).

3β-*Acetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α-*pregnan*-20-*one* (IV).—A solution of 3β-acetoxy-16β-methyl-5α-pregn-9-en-20-one (V) (1·89 kg.) in methylene chloride (20·0 l.) was stirred with 10% sodium acetate solution (2 l.) and cooled in ice–salt. Chlorine was passed in during 10½ min. at 11·6 l./min. Excess of chlorine appeared in the solution at this time, and the gas flow was continued for a further 1 min. The temperature of the mixture rose from 5·5° to 18·5°. Sodium hydrogen carbonate (500 g.) in water (5·0 l.) was added and the mixture stirred until the excess of chlorine had disappeared. The organic layer was washed with water and evaporated to dryness at room temperature. The crystalline residue recrystallised from boiling acetone (10·0 l.) to which water (3·0 l. at 55°) was added, to give the crude product (1·965 kg., 83·3%), m. p. 164—165°, $[\alpha]_D$ +46·4°. Recrystallisation from ethyl acetate gave the 9α,11β-*dichloro-ketone*, m. p. 168—169°, $[\alpha]_D$ +48·8° (Found: C, 65·0; H, 8·3; Cl, 16·1. $C_{24}H_{36}Cl_2O_3$ requires C, 65·0; H, 8·2; Cl, 16·0%), $\nu_{max.}$ 1732 and 1240 (OAc), 1710 (C=O), and 750 and 660 cm.$^{-1}$ (9,11-Cl_2).

3β-*Acetoxy*-16β-*methyl*-5α-*pregna*-9,17-*dien*-20-*ol* (VIII).—A solution of 3β-acetoxy-16-methyl-5α-pregna-9,16-dien-20-one (100 g.) in tetrahydrofuran (1200 ml.) and triethylamine (200 ml.) was hydrogenated over 10% palladised charcoal (8·5 g.) (uptake 6·5 l. in 9 min.). The solution was filtered cold and evaporated to a dry solid without excessive heating. The residue was suspended in acetone (200 ml.) and the insoluble material filtered off, washed with acetone (3 × 50 ml.), and dried at 60° *in vacuo* to give the crude product (27·8 g.), m. p. 133—136°. A further treatment with boiling acetone (500 ml.) gave the *enol* (VIII) (20·8 g., 20·7%), m. p. 134—140°, $[\alpha]_D$ +30·6°, +30·3° (in dioxan) (Found: C, 77·3; H, 9·7; active H, 0·21. $C_{24}H_{36}O_3$ requires C, 77·4; H, 9·7; active H, 0·27%). The ultraviolet spectrum showed a rapidly increasing absorption at decreasing wavelength; at 220 mμ $E^{1\%}_{1cm.}$ was 102. $\nu_{max.}$ (Nujol) were at 3480 (bonded OH), 1716 and 1265 (OAc), 824 (>C=CH–), and 1690 cm.$^{-1}$ (O·C=C). The specimen was stable in Nujol but changed steadily in CS_2. As a comparison 3β-acetoxy-16β-methyl-5α-pregn-9-en-20-one showed no active H, and at 220 mμ $E^{1\%}_{1cm.}$ was 5; no 3480 cm.$^{-1}$ band was visible.

When the enol was heated at 100° *in vacuo* for 2 hr. it slowly sintered but it solidified on cooling. A sample recrystallised from methanol then had m. p. 111—115°, $[\alpha]_D$ +20·1°; the infrared spectrum showed it to be a mixture of 17α- and 17β-20-ketones.

Mild Acetylation of the Enol.—The enol (2·0 g.) was suspended in dry pyridine (5·0 ml.) and

XUM

acetic anhydride (5·0 ml.) under nitrogen. After 4 hr. at room temperature, a clear solution had been formed and after a further 2 hr. this was evaporated to dryness at 40°/0·5 mm. Crystallisation of the crystalline residue from methanol gave two crops: (1) needles (0·93 g., 41·8%), m. p. 158—160°, $[\alpha]_D$ +34·1°, whose infrared spectrum suggested the presence of the enol acetate group; (2) needles (0·42 g.), m. p. 115—138°, $[\alpha]_D$ +33·7°, whose infrared spectrum showed it to be largely the 20-ketone (1712 cm.$^{-1}$). Recrystallisation of crop (1) from methanol gave the enol acetate (VIIIa) (see below), m. p. 164—166°, $[\alpha]_D$ +34°, the infrared spectrum showing the absence of ketone.

Rearrangement of the Enol.—(*a*) The enol (0·2678 g.) in air-free tetrahydrofuran under nitrogen (total vol. 20·0 ml. at 20°) showed $[\alpha]_D$ +30·6°. This solution was treated with 0·1N-sodium hydroxide in methanol (0·20 ml.). $[\alpha]_D$ fell to 22·4° in less than 30 sec. and was constant (20 min.) after that time. The solution was neutralised with aqueous 0·1N-hydrochloric acid (0·20 ml.) and evaporated to dryness *in vacuo* at room temperature. The infrared spectrum (Nujol mull) showed the product to contain <10% of hydroxyl group (3450 cm.$^{-1}$), indicating that rearrangement to the lower rotating 17α-acetyl compound (Va) as well as to (V) had occurred. (*b*) Treatment of a similar solution to that used in (*a*) with aqueous 0·1N-hydrochloric acid produced no change in the optical rotation of the solution except that due to the slight dilution. The solution was neutralised and evaporated to dryness. The infrared spectrum (Nujol mull) showed <10% of hydroxyl group (3450 cm.$^{-1}$). Rearrangement to the 17β-acetyl compound (V) had thus occurred. (*c*) A sample of the corresponding ketone (V) in tetrahydrofuran showed no change in rotation on treatment with either acid or alkali as under (*a*) and (*b*). (*d*) The enol in air-free tetrahydrofuran (1% solution) was left at room temperature for 30 min. under nitrogen. The solution was evaporated to dryness under reduced pressure at room temperature. The residue showed a slight drop in m. p. and some change in the infrared spectrum (Nujol). (*e*) Tetrahydrofuran (7·0 ml.) containing 14% v/v of triethylamine was flushed with nitrogen, and enol (0·5 g.) and activated charcoal (1·0 g.) (previously washed neutral with water and dried) were added. The suspension was stirred under nitrogen for 30 min. at room temperature, then filtered, and the filtrate was evaporated to dryness at room temperature under reduced pressure, giving a crystalline solid, m. p. 88—94°, $[\alpha]_D$ +31·8°, whose infrared spectrum (Nujol) showed <10% of enol form. Rearrangement to the 17β-acetyl compound (V) was therefore very largely complete.

Oxygenation of 3β-*Acetoxy*-16β-*methyl*-5α-*pregna*-9,17-*dien*-20-*ol* (VIII) (with Miss E. J. Bailey).—The enol (2·0 g.) was dissolved in benzene (200 ml.) by warming. The solution was cooled to room temperature and shaken with oxygen until 1 mol. had been absorbed. The benzene was removed under reduced pressure to give a white solid (2·2 g.), m. p. 120—123°, $[\alpha]_D$ +36° (in MeOH). Crystallisation from aqueous methanol gave 3β-*acetoxy*-17α-*hydroperoxy*-16β-*methyl*-5α-*pregn*-9-*en*-20-*one* (0·95 g.) in two crops. The analytical specimen had m. p. 161—164° (decomp.) (Kofler), $[\alpha]_D$ +57° (in MeOH) (Found: C, 71·1; H, 9·1. $C_{24}H_{36}O_5$ requires C, 71·5; H, 9·0%), $\nu_{max.}$ (in Nujol) 1730 and 1245 (OAc), 1700 (C=O) and 820 cm.$^{-1}$ (>C=CH–).

3β-*Acetoxy*-16β-*methyl*-5α,17α-*pregn*-9-*en*-20-*one* (Va).—3β-Acetoxy-16β-methyl-5α-pregn-9-en-20-one (V) (0·4 g.) in chloroform (20 ml.) was treated with 9·5N-hydrogen chloride in anhydrous ethanol (0·226 ml.). α_D of the solution dropped from +1·20° to −1·33° during 35 min. and then remained constant. The solution was poured into 2% sodium hydrogen carbonate solution (150 ml.), and the chloroform layer washed and evaporated to give a solid which on crystallising from 80% methanol gave the 17α-*compound* (0·23 g., 57·5%), m. p. 121°, $[\alpha]_D$ −41° (Found: C, 77·2; H, 9·9. $C_{24}H_{36}O_3$ requires C, 77·4; H, 9·75%), $\nu_{max.}$ (in CS_2) 1732 and 1240 (OAc), 1705 (C=O), and 822 cm.$^{-1}$ (9-C:C).

3β-*Acetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α,17α-*pregnan*-20-*one* (IVa).—3β-Acetoxy-9α,11β-dichloro-16β-methyl-5α-pregnan-20-one (IV) (5·0 g.) in chloroform (250 ml.) was treated with 9·5N-hydrogen chloride in anhydrous ethanol (2·4 ml.). α_D of the solution fell from +1·71° to −0·13° in 2½ hr. (constant). The product (4·9 g.), m. p. 160—167°, $[\alpha]_D$ −4·2°, obtained as in the previous experiment, crystallised from 75% acetone to give 3β-*acetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α,17α-*pregnan*-20-*one* as prisms, m. p. 173—174°, $[\alpha]_D$ −4·2° (Found: C, 64·9; H, 8·4; Cl, 15·85. $C_{24}H_{36}Cl_2O_3$ requires C, 65·0; H, 8·2; Cl, 16·0%), $\nu_{max.}$ 1732 and 1240 (OAc), 1705 (C=O) and 754 and 660 cm.$^{-1}$ (9,11-Cl_2).

3β,20-*Diacetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α-*pregn*-17-*ene* (VII).—(a) *From* 3β-*acetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α-*pregnan*-20-*one* (IV). To the 20-ketone (5·0 g.) in carbon

tetrachloride (25 ml.) was added, with stirring and cooling, acetic anhydride (17 ml.) containing 60% perchloric acid (0·35 ml.). The mixture was left at room temperature for 2 hr., then water (3·0 ml.) was added dropwise with stirring and cooling. The organic layer was washed and evaporated to a gum which, on trituration with light petroleum (b. p. 40—60°) (15 ml.) and cooling, yielded a solid (3·1 g., 56·6%), m. p. 159—163°, $[\alpha]_D$ +55·5°. Recrystallisation from light petroleum gave a product identical with the analytical specimen of the enol acetate described in experiment (b).

(b) *From* 3β,20-*diacetoxy*-16β-*methyl*-5α-*pregna*-9,17-*diene* (VIIIa) (*isomer "A"*; *see below*). The enol acetate (75·3 g.) in carbon tetrachloride (750 ml.) at −9° was treated with 1·96N-chlorine in carbon tetrachloride (190 ml.) during 3 min., the temperature rising to 0°. The solvent was removed under reduced pressure and the residue crystallised from light petroleum (b. p. 100—120°; 186 ml.), to give a crude product (51·5 g., 58·4%), m. p. 167—170°, $[\alpha]_D$ +53·5°. Two further crystallisations from light petroleum gave 3β,20-*diacetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α-*pregn*-17-*ene* (this compound was designated *isomer "A"*), m. p. 174—179°, $[\alpha]_D$ +55·1° (Found: C, 64·2; H, 8·2; Cl, 14·2. $C_{35}H_{38}Cl_2O_4$ requires C, 64·3; H, 7·9; Cl, 14·6%), $\nu_{max.}$ 1745 and 1216 (enol-acetate), 1735 and 1240 (OAc), 754 and 654 cm.$^{-1}$ (9,11-Cl_2).

The corresponding 20-isomer (designated *isomer "B"*) was obtained in a similar manner from 3β,20-diacetoxy-16β-methyl-5α-pregna-9,17-diene (isomer "B"; see below) in 37% yield, as prisms, m. p. 179—186°, $[\alpha]_D$ +57·8° (Found: C, 64·4; H, 8·1; Cl, 14·5%), $\nu_{max.}$ 1745 and 1212 (enol acetate), 1735 and 1240 (OAc) and 752 and 650 cm.$^{-1}$ (9,11-Cl_2).

3β,20-*Diacetoxy*-16β-*methyl*-5α-*pregna*-9,17-*diene* (VIIIa).—3β-Acetoxy-16β-methyl-5α-pregn-9-en-20-one (V) (10 g.) in carbon tetrachloride (25 ml.) was treated with a mixture (8·5 ml.) of acetic anhydride (10 ml.) and 60% perchloric acid (0·05 ml.) with stirring. The solution, which darkened rapidly, was set aside for 1 hr. at room temperature and water (1·5 ml.) was then added with cooling and stirring. The organic layer was washed and evaporated under reduced pressure (finally from methanol), to give crystals (8·30 g., 74·6%), m. p. 148—157°, $[\alpha]_D$ +33·8°. Recrystallisation several times from acetone gave 3β,20-*diacetoxy*-16β-*methyl*-5α-*pregna*-9,17-*diene*, m. p. 162—165°, $[\alpha]_D$ +34·2° (Found: C, 75·4; H, 9·3. $C_{36}H_{38}O_4$ requires C, 75·3; H, 9·2%), $\nu_{max.}$ (in CS_2) 1745 and 1225 (enol acetate), 1735 and 1240 (OAc), 822 (9-C:C) and 1696 cm.$^{-1}$ ($\Delta^{17(20)}$). This compound was designated isomer "A".

From a similar experiment (20-g. scale) a second crop (3·14 g., 14·1%) of low-melting solid with $[\alpha]_D$ +38·3° was obtained which after three recrystallisations from methanol gave a compound formulated as the 20-stereoisomer of (VIIIa), m. p. 120—136°, $[\alpha]_D$ +45·8° (in $CHCl_3$) (Found: C, 75·2; H, 9·4%). This compound was designated *isomer "B."*

3β,20-*Diacetoxy*-9α,11β-*dichloro*-17α,20-*epoxy*-16β-*methyl*-5α-*pregnane* (IX).—3β,20-Diacetoxy-9α,11β-dichloro-16β-methylpregn-17-ene (VII) (10 g.) (isomer "A") in chloroform (25 ml.) was treated with 2·4N-monoperphthalic acid in ether (26·5 ml.) at room temperature. The temperature rose to 26·5° after ¾ hr. Next morning the precipitated phthalic acid was filtered off and dissolved in aqueous 2N-sodium hydroxide (24 ml.), and this solution was extracted with chloroform. The combined organic layers were worked up as usual. The product crystallised from acetone (100 ml.) to give a first crop (8·54 g., 82·7%), m. p. 163—165°, $[\alpha]_D$ +68·0°, and a second crop (0·82 g., 7·94%), m. p. 161—162°, $[\alpha]_D$ +61·3°. A sample was recrystallised from acetone to give the 17α,20-*epoxide* (*"A" isomer*) as prisms, m. p. 164—165°, $[\alpha]_D$ +68·0° (Found: C, 62·2; H, 7·9; Cl, 14·2. $C_{36}H_{38}Cl_2O_5$ requires C, 62·3; H, 7·6; Cl, 14·1%), $\nu_{max.}$ 1755 and 1240 (epoxy-acetate), 1742 and 1240 (OAc), and 750 and 658 cm.$^{-1}$ (9,11-Cl_2).

The "B" isomer of the enol acetate was epoxidised similarly, to yield the 17α,20-*epoxide* (*"B" isomer*), m. p. 180—181°, $[\alpha]_D$ +48·2° (Found: C, 61·8; H, 7·8; Cl, 13·9%), $\nu_{max.}$ 1755 and 1240, 1742 and 1240, and 750 and 658 cm.$^{-1}$. The spectra of the isomers differed in the finger-print region.

9α,11β-*Dichloro*-3β,17-*dihydroxy*-16β-*methyl*-5α-*pregnan*-20-*one* (XII) *from* 3β,20-*Diacetoxy*-9α,11β-*dichloro*-17α,20-*epoxy*-16β-*methyl*-5α-*pregnane* (IX).—(a) *From the "A" isomer.* The dichloro-diacetate epoxide (10 g.) was left in glacial acetic acid (300 ml.) containing concentrated sulphuric acid (2·95 ml.) and water (20 ml.) at room temperature for 3 hr., then poured into water (2 l.). The steroid was extracted with methylene chloride which was evaporated off under reduced pressure and replaced by light petroleum (b. p. 100—120°). This gave needles (7·2 g., 78·6%), m. p. 180° (decomp.), $[\alpha]_D$ +46°. A sample recrystallised from acetone

XUM

gave 3β-*acetoxy*-9α,11β-*dichloro*-17-*hydroxy*-16β-*methyl*-5α-*pregnan*-20-*one* (XIIa), m. p. 183° (decomp.), $[\alpha]_D$ +46·5°, +65·5° (in dioxan) (Found: C, 63·05; H, 7·8; Cl, 15·5. $C_{24}H_{36}Cl_2O_4$ requires C, 62·7; H, 7·9; Cl, 15·4%), $\nu_{max.}$ (in CS_2) 1738 and 1240 (OAc), 1710 and 1678 cm.$^{-1}$ (20-C=O).

This acetate (5·0 g.) in methylene chloride (62·5 ml.) and methanol (54 ml.) was mixed with a solution of concentrated sulphuric acid (11·25 ml.) in water (11·25 ml.) and methanol (54 ml.), then kept at room temperature for 16 hr. The crystalline product was filtered off, washed, and dried *in vacuo* at 60° {0·69 g., 15·2%; m. p. 196° (decomp.), $[\alpha]_D$ +75·2° (in dioxan)}. Diluting the filtrate with water gave a further precipitate (3·05 g., 67·1%), m. p. 198° (decomp.), $[\alpha]_D$ +75·4° (in dioxan). A sample recrystallised from tetrahydrofuran gave the 3β,17-*diol*, m. p. 207° (decomp.), $[\alpha]_D$ +77·1° (in dioxan) (Found: C, 63·2; H, 8·2; Cl, 16·8. $C_{22}H_{24}Cl_2O_3$ requires C, 63·3; H, 8·2; Cl, 17·0%), $\nu_{max.}$ (in Nujol) 1684 (C=O) and 752 and 662 cm.$^{-1}$ (9,11-Cl_2).

The epoxide diacetate (" A " isomer) was also hydrolysed directly to the 3β,17-*diol* in aqueous methanol–sulphuric acid as above, or better by treating a solution (5·0 g.) in methylene chloride (25 ml.) with potassium hydroxide (1·32 g.) in methanol (35 ml.) and water (2·0 ml.) for 1½ hr. at room temperature. The crystalline product was dried *in vacuo* at 60° {4·02 g., 96·5%; m. p. 200—203° (decomp.), $[\alpha]_D$ +75° (in dioxan)}; its infrared spectrum was identical with that of the authentic specimen.

(b) *From the " B " isomer.* The epoxide diacetate " B " isomer was treated with aqueous methanol–sulphuric acid as for the 3-acetate above, yielding the 3β,17-diol (86%), m. p. 196° (decomp.), $[\alpha]_D$ +76·8° (in dioxan), identical in its infrared spectrum with the authentic specimen.

3β-*Acetoxy*-17aβ-*hydroxy*-16ξ,17aα-*dimethyl*-D-*homo*-5α-*pregn*-9-*en*-17-*one* (XIX).—3β,17-Dihydroxy-16β-methyl-5α-pregn-9-en-20-one (XIII) (1·0 g.) was added to methanol (10 ml.) containing 50% aqueous sulphuric acid (0·2 ml.), and the solution refluxed for 10 hr. The clear solution was poured into water (120 ml.), and the product isolated with chloroform. The solvent was evaporated under reduced pressure and the residual gum was left in pyridine (3 ml.) and acetic anhydride (3 ml.) at 60° for 1 hr. This gave (after three crystallisations from methanol) the D-*homo*-*steroid* (0·218 g.), m. p. 153—155°, $[\alpha]_D$ −81° (in dioxan) (Found: C, 74·4; H, 9·4. $C_{24}H_{36}O_4$ requires C, 74·3; H, 9·35%), $\nu_{max.}$ 1732 and 1240 (OAc), 1708 (C=O), and 820 cm.$^{-1}$ (9-C=C).

3β-*Acetoxy*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*en*-20-*one* (XIIIa).—10% Palladium oxide on charcoal (1·4 g.) was prereduced under hydrogen in tetrahydrofuran (35 ml.). 3β-Acetoxy-9α,11β-dichloro-17-hydroxy-16β-methyl-5α-pregnan-20-one (XIIa) (7·0 g.) in tetrahydrofuran (70 ml.) containing triethylamine (6·35 ml.) was then added and hydrogenation continued until uptake ceased (392 ml., 1·045 mol.) after 35 min. The catalyst was filtered off and washed with methylene chloride, and the combined filtrate and washings were washed with water. Evaporation of the organic phase gave a product (4·11 g., 69·5%), m. p. 175—177° (from methanol), $[\alpha]_D$ +32·6° (dioxan). Two further crystallisations gave 3β-*acetoxy*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*en*-20-*one* as plates (2·96 g., 42%), m. p. 177—179°, $[\alpha]_D$ +3·9°, +34·1° (in dioxan) (Found: C, 73·9; H, 9·45. $C_{24}H_{36}O_4$ requires C, 74·2; H, 9·35%), $\nu_{max.}$ 1735 and 1240 (OAc), 1710 and 1680 (20-C=O), and 820 cm.$^{-1}$ (9-C=C).

3β,17-*Dihydroxy*-16β-*methyl*-5α-*pregnan*-20-*one* (XIV).—10% Palladium oxide on charcoal (0·7 g.) was prereduced under hydrogen in glacial acetic acid. 3β-Acetoxy-17-hydroxy-16β-methyl-5α-pregn-9-en-20-one (XIIIa) (1·0 g.) was added in acetic acid (30 ml.) and hydrogenation continued until the uptake ceased (21 hr.; 66·5 ml., 1·05 mol.). The catalyst was filtered off and the product precipitated with water, collected, washed, and dried (0·96 g.; m. p. 161—163°). Two crystallisations from methanol afforded 3β-acetoxy-17-hydroxy-16β-methyl-5α-pregnan-20-one (XIVa) (0·65 g.), m. p. and mixed m. p. 162—164°, $[\alpha]_D$ +38·5° (in dioxan), $\nu_{max.}$ 1735 and 1245 (OAc), and 1712 and 1680 cm.$^{-1}$ (C=O) (cf. the authentic specimen, m. p. 164—166°). We are indebted to Schering Corporation for authentic samples of compounds (XIV) and (XIVa).

The 3β-acetate (0·43 g.) was hydrolysed by refluxing it in methanol (25·5 ml.) containing water (5·1 ml.) and potassium hydrogen carbonate (0·255 g.) for 1 hr. The product (0·375 g., 97·7%) was isolated by precipitation but could not be purified by crystallisation. The crude material was kept overnight in methanol (40 ml.) containing 50% aqueous sulphuric acid (5·1 ml.). The crystalline product which separated was filtered off, washed, and dried to give

the saturated diol (XIV) (0·25 g., 65·2%), m. p. and mixed m. p. 216—221°, $[\alpha]_D$ +45·5° (in dioxan) (Found: C, 75·6; H, 10·3. Calc. for $C_{22}H_{36}O_3$: C, 75·8; H, 10·4%), $\nu_{max.}$ (in Nujol) 1690 cm.$^{-1}$ (C=O) (authentic specimen, m. p. 212—217°, $[\alpha]_D$ +43° in dioxan).

17β-*Acetoxy*-9α,11β-*dichloro*-3β-*hydroxy*-16β-*methyl*-5α,17α-*pregnan*-20-*one* (X).—The mother-liquors from the acid-catalysed hydrolysis in aqueous methanol of 3β,20-diacetoxy-9α,11β-dichloro-17α,20-epoxy-16β-methyl-5α-pregnane (isomer "A") (IX) (113 g.) were evaporated under reduced pressure to remove as much of the remaining methylene chloride as possible. The residual gum was refluxed with ethyl acetate, and the precipitated white solid (7·47 g.) filtered off and washed with hot ethyl acetate. This material, m. p. 187—193° (decomp.), $[\alpha]_D$ +64° (dioxan), was identified as the dichloro-diol (XII) by its constants and infrared spectrum. The filtrate was cooled and allowed to crystallise {6·6 g., 6·38%; m. p. 200—203° (decomp.), $[\alpha]_D$ +49° (in dioxan)}. Recrystallisation from ethyl acetate–methylene chloride (1 : 1) gave the 17β-*acetate* as flat needles, m. p. 203—204° (decomp.), $[\alpha]_D$ +47° (dioxan) (Found: C, 62·8; H, 7·7; Cl, 15·3. $C_{24}H_{36}Cl_2O_4$ requires C, 62·7; H, 7·9; Cl, 15·4%), $\nu_{max.}$ 1738 and 1244 (OAc), 1710 (C=O), and 670 and 758 cm.$^{-1}$ (9,11-Cl_2) (absence of the 17-hydroxy-20-oxo-system).

3β,17β-*Diacetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α,17α-*pregnan*-20-*one* (Xa).—(a) *From* 17β-*acetoxy*-9α,11β-*dichloro*-3β-*hydroxy*-16β-*methyl*-5α,17α-*pregnan*-20-*one* (X). The steroid (4·37 g.) was suspended in carbon tetrachloride (30 ml.), and acetic anhydride (10 ml.) containing 60% perchloric acid (0·03 ml.) was added. The mixture was shaken for 3 min., the starting material dissolving and the product separating. The mixture was left for 12 min. and water (1·3 ml.) was slowly added while the temperature was kept below 45°. The product (4·0 g.) was filtered off and washed with acetone. Crystallisation of this material (3·0 g.) from methylene chloride–acetone gave the 3β,17β-*diacetate* as prisms (2·59 g., 72·4%), m. p. 229—232° (decomp.), $[\alpha]_D$ +34° (Found: C, 62·2; H, 7·7; Cl, 14·1. $C_{26}H_{38}Cl_2O_5$ requires C, 62·3; H, 7·6; Cl, 14·1%), $\nu_{max.}$ (in Nujol) 1738—1730 and 1254—1240 (OAc), 1710 (C=O), and 756 and 664 cm.$^{-1}$ (9,11-Cl_2).

(b) *From* 3β,20-*diacetoxy*-9α,11β-*dichloro*-17α,20-*epoxy*-16β-*methyl*-5α-*pregnane* (*isomer "A"*) (IX) *by acid catalysis*. The diacetate epoxide (13·0 g.) in methylene chloride (52 ml.) was treated with acetic acid (720 ml.) containing concentrated sulphuric acid (3·8 ml.) and water (13 ml.) at room temperature for 3 hr., after dilution of the solution with water and extraction with chloroform, a crystalline product (6·78 g., 56·9%) was obtained by adding light petroleum (b. p. 100—120°) to the chloroform extract and cooling it at −5° overnight. This was identified as 3β-acetoxy-9α,11β-dichloro-17-hydroxy-16β-methyl-5α-pregnan-20-one (XIIa) by its constants {m. p. 181—183° (decomp.), $[\alpha]_D$ +65° (in dioxan), and infrared spectrum}. A second crop (4·15 g., 34·9%) had m. p. 171—176° (decomp.), $[\alpha]_D$ +59·6° (in dioxan), and an infrared spectrum showing it to be a mixture of the above 3β-acetate and the 3β,17β-diacetate (Xa). This mixture was refluxed with acetone and the insoluble material discarded. Three crops (total 1·25 g.) obtained from the filtrate recrystallised from acetone to give the 3β,17β-diacetate, m. p. 219° (decomp.), $[\alpha]_D$ +34·5°, +42° (in dioxan) (correct infrared spectrum).

(c) *From* 3β,20-*diacetoxy*-9α,11β-*dichloro*-17α,20-*epoxy*-16β-*methyl*-5α-*pregnane* (isomer "*A*") (IX) *by heat*. The diacetate epoxide (6·5 g.) was heated in an open boiling-tube at 185° for 10 min. with stirring. The solid melted slowly to a cloudy liquid and then began to recrystallise. The cold mixture was suspended in acetone. The insoluble material was filtered off, washed with acetone, and recrystallised from acetone–methylene chloride, to give the 3β,17β-diacetate (1·3 g., 20%), m. p. 226° (decomp.), $[\alpha]_D$ +36·5° (correct infrared spectrum).

3β,17-*Diacetoxy*-9α,11β-*dichloro*-16β-*methyl*-5α-*pregnan*-20-*one* (XIIb).—9α,11β-Dichloro-3β,17-dihydroxy-16β-methyl-5α-pregnan-20-one (XII) (5·0 g.) was suspended in carbon tetrachloride (30 ml.), and acetic anhydride (10 ml.) containing 60% w/w perchloric acid (0·03 ml.) was added. The mixture was shaken for 3 min. and left for 12 min. at room temperature. Water (1·3 ml.) was added slowly, the temperature being kept below 45°. The solution was washed and evaporated. The yellow residue recrystallised from acetone as needles (3·11 g., 51·8%), m. p. 170—190° (decomp.), $[\alpha]_D$ +60°. A second recrystallisation from acetone gave the 3β,17-*diacetate* as needles (1·08 g., 18·0%), m. p. 225—228° (decomp.), $[\alpha]_D$ +59·5° (Found: C, 62·3; H, 7·7; Cl, 14·4%), $\nu_{max.}$ 1735 and 1240 (OAc), 1718 (C=O), and 754 and 662 cm.$^{-1}$ (9,11-Cl_2).

3β,17β-*Diacetoxy*-16β-*methyl*-5α,17α-*pregn*-9-*en*-20-*one* (XIa).—17β-Acetoxy-9α,11β-dichloro-3β-hydroxy-16β-methyl-5α,17α-pregnan-20-one (X) (4·0 g.), suspended in acetic acid (39 ml.) containing sodium acetate (2·3 g.), was stirred with zinc dust (7·7 g.; washed with mineral acid,

water, and methanol and dried) at 24—30° for 4 hr. The zinc was filtered off and water added to the filtrate to precipitate the 3-hydroxy-compound (3·17 g., 93·7%), m. p. 215—217°, $[\alpha]_D$ +5°. The 3β-hydroxyl group was acetylated in pyridine (10 ml.) and acetic anhydride (5 ml.) at 50° for 1 hr., to give the crude *diacetate* (3·25 g., 98%), m. p. 154—155°, $[\alpha]_D$ +8·3° (in dioxan). The pure compound was obtained, after two recrystallisations from methanol, as prisms, m. p. 156—157°, $[\alpha]_D$ +6·2°, +9·6° (in dioxan) (Found: C, 72·5; H, 9·0. $C_{26}H_{38}O_5$ requires C, 72·6; H, 9·0%), $\nu_{max.}$ 1738 and 1246 (OAc), 1716 (C=O) and 822 cm.$^{-1}$ (9-C:C).

3β,17-*Diacetoxy*-16β-*methyl*-5α-*pregn*-9-*en*-20-*one* (XIIIb).—3β,17-Diacetoxy-9α,11β-dichloro-16β-methyl-5α-pregnan-20-one (XIIb) (6·0 g.) was treated with zinc dust as in the previous experiment, to give the Δ^9-*compound*, m. p. 156—158°, $[\alpha]_D$ +23·2°, +20° (in dioxan) (Found: C, 72·3; H, 8·9%), $\nu_{max.}$ 1736 and 1246 (OAc), 1722 (C=O), and 822 cm.$^{-1}$ (9-C:C).

21-*Acetoxy*-9α,11β-*dichloro*-3β,17-*dihydroxy*-16β-*methyl*-5α-*pregnan*-20-*one* (XVa).—A 9·2N-solution (110 ml.) of hydrogen chloride in ethanol was added to a suspension of 9α,11β-dichloro-3β,17-dihydroxy-16β-methyl-5α-pregnan-20-one (XII) (60 g.) in chloroform (1·2 l.) and the mixture stirred for 15 min. Bromine (23·5 g.) in chloroform (150 ml.) was then added at such a rate that the bromine was never in great excess. Saturated aqueous sodium hydrogen carbonate solution (920 ml.) was cautiously added and the precipitate was isolated and dried at 45° for 15 hr., to give 21-bromo-9α,11β-dichloro-3β,17-dihydroxy-16β-methyl-5α-pregnan-20-one (57·6 g., 81%), m. p. 185° (decomp.), $[\alpha]_D$ +89° (*c* 0·5 in dioxan). Total halogen: 7·622 mg. gave 7·3% of Ag halide; $C_{22}H_{33}BrCl_2O_3$ requires 7·3%.

The 21-bromide (57·6 g.) was refluxed in acetone (1·3 l.) with anhydrous potassium acetate (142 g.) for 2 hr. The inorganic salts were removed by filtration of the hot solution, the filtrate concentrated to low bulk under reduced pressure, and the product precipitated by addition of water (1·2 l.), yielding 21-*acetoxy*-9α,11β-*dichloro*-3β,17-*dihydroxy*-16β-*methyl*-5α-*pregnan*-20-*one* (55 g.), m. p. 167° (decomp.), $[\alpha]_D$ +95° (in dioxan). Recrystallisation from acetonitrile gave pure material, m. p. 173° (decomp.), $[\alpha]_D$ +100° (in dioxan) (Found: Cl, 14·65. $C_{24}H_{36}O_5Cl_2$ requires Cl, 14·95%). $\nu_{max.}$ (in Nujol) 1735 and 1264 (21-OAc), 1718 (20-C=O), and 754 and 668 cm.$^{-1}$ (9,11-Cl_2).

Dechlorination of 21-*Acetoxy*-9α,11β-*dichloro*-3β,17-*dihydroxy*-16β-*methyl*-5α-*pregnan*-20-*one* (XVa).—(a) *By palladium–charcoal.* The dichloro-compound (57·6 g.) in tetrahydrofuran (290 ml.), water (29 ml.), and triethylamine (49 ml.) was hydrogenated on 10% palladium–charcoal (14 g.) (uptake, 285 ml. in 50 min.). The catalyst was filtered off and the product precipitated by addition of water (1·0 l.) to the concentrated filtrate, and was dried at 40—45° for 16 hr., to yield 21-*acetoxy*-3β,17-*dihydroxy*-16β-*methyl*-5α-*pregn*-9-*en*-20-*one* (XVI) (48·3 g., 98%), m. p. 192—194°, $[\alpha]_D$ +59° (*c* 0·5 in dioxan). Material recrystallised from methanol and again from ethyl acetate had m. p. 197—198°, $[\alpha]_D$ +61·8° (*c* 0·5 in dioxan) (Found: C, 71·1; H, 9·0. $C_{24}H_{36}O_5$ requires C, 71·3; H, 9·0%), $\nu_{max.}$ (in $CHBr_3$) 1744 and 1236 (21-OAc), 1726 (20-C=O), and 820 cm.$^{-1}$ (9-C:C), $\nu_{max.}$ (in Nujol) 1746 and 1236, 1722, and 820 cm.$^{-1}$. When the sample was precipitated from acetic acid by water and dried at 60° *in vacuo* the bands in the Nujol spectrum were displaced to 1728 and 1266 (21-OAc), 1728 (20-C=O), and 818 cm.$^{-1}$ (9-C:C), and the bromoform spectrum showed the presence of water at 1600 cm.$^{-1}$.

(b) *By chromous chloride.* 2·2N-Chromous chloride (2·0 ml.) was added to the dichloro-ketone (1·0 g.) in acetic acid (10 ml.) under an inert atmosphere. The solution was poured into water (100 ml.), and the product extracted in methylene chloride (2 × 50 ml.). The bulked extracts were washed with sodium hydrogen carbonate solution (2 × 50 ml.) and water (2 × 50 ml.). The solvent was distilled off under reduced pressure and the residue diluted with water (50 ml.). The solid was collected and dried *in vacuo* at 100°, to give 21-acetoxy-3β,17α-dihydroxy-16β-methyl-5α-pregn-9-en-20-one (0·72 g.), m. p. 183—189°, $[\alpha]_D$ +63° (*c* 0·48 in dioxan).

(c) *By zinc dust.* The dichloro-compound (1 g.) in acetic acid (25 ml.) was stirred with zinc dust (0·2 g.) at room temperature overnight. The product (0·57 g.), isolated by dilution with water (250 ml.), had m. p. 186—194°, $[\alpha]_D$ +62° (*c* 0·5 in dioxan).

21-*Acetoxy*-9α,11β-*dichloro*-17-*hydroxy*-16β-*methyl*-5α-*pregnane*-3,20-*dione* (XVII).—Anhydrous sodium acetate (52·8 g.) in acetic acid (880 ml.) was stirred with 21-acetoxy-9α,11β-dichloro-3β,17-dihydroxy-16β-methyl-5α-pregnan-20-one (50 g.) in methylene chloride (208 ml.) while chlorine gas was bubbled in at room temperature until 2 mol. had been absorbed (10 min.). The reaction was completed by stirring the mixture for ½ hr. and then setting it aside overnight at room temperature. Water (830 ml.) was added, the organic layer separated, and the aqueous

layer extracted with methylene chloride (3 × 125 ml.). The extracts were bulked and the resulting solution was washed with 1% aqueous sodium pyrosulphite solution (1 × 400 ml.), water (2 × 25 ml.), aqueous sodium hydrogen carbonate (1 × 250 ml.), and water (1 × 250 ml.). The solvent was evaporated under reduced pressure until crystallisation commenced; light petroleum (b. p. 100—120°; 100 ml.) was added and then the evaporation of the methylene chloride was completed. The solid was filtered off and dried *in vacuo* at 60° for 4 hr., to yield 21-*acetoxy*-9α,11β-*dichloro*-17-*hydroxy*-16β-*methyl*-5α-*pregnane*-3,20-*dione* (46·5 g.), m. p. 180° (decomp.), $[\alpha]_D$ +102° (in dioxan) (Found: C, 60·7; H, 7·3; Cl, 15·4. $C_{24}H_{34}Cl_2O_5$ requires C, 60·9; H, 7·2; Cl, 15·0%).

21-*Acetoxy*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*ene*-3,20-*dione* (XVIII).—(a) *By oxidation of* 21-*acetoxy*-3β,17-*dihydroxy*-16β-*methyl*-5α-*pregn*-9-*en*-20-*one* (XVI). The steroid (2·0 g.) in acetone at 50° was agitated and treated with an oxidising mixture (6·1 ml., from 110·8 g. of potassium dichromate per l. of 3N-sulphuric acid) for 15 min. The mixture was concentrated to ~15 ml. and water (200 ml.) added to precipitate the crude product (1·80 g.), m. p. 184—189°. Recrystallisation from acetone gave pure 21-*acetoxy*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*ene*-3,20-*dione*, m. p. 191—193°, $[\alpha]_D$ +81° (*c* 0·5 in dioxan), R_F 0·63 (Zaffaroni-type system) (Found: C, 71·4; H, 8·8. $C_{24}H_{34}O_5$ requires C, 71·6; H, 8·5%), $\nu_{max.}$ 1744 and 1230 (21-OAc), 1726 (20-C=O), and 1706 cm.$^{-1}$ (C=O).

(b) *By dechlorination of* 21-*acetoxy*-9α,11β-*dichloro*-17-*hydroxy*-16β-*methyl*-5α-*pregnane*-3,20-*dione* (XVII). The steroid (10·6 g.) in tetrahydrofuran (106 ml.), dimethylacetamide (120 ml.), and triethylamine (9·27 ml.) was hydrogenated with 5% palladium oxide on kieselguhr (5·3 g.) at atmospheric pressure. Hydrogen uptake (650 ml.) stopped after 30 min. The catalyst was filtered off, the tetrahydrofuran evaporated under reduced pressure, and the product precipitated by water (620 ml.), to give 21-acetoxy-17-hydroxy-16β-methyl-5α-pregn-9-ene-3,20-dione (8·43 g.), m. p. 189—193°, $[\alpha]_D$ +81·2° (*c* 0·5 in dioxan). The infrared spectrum resembled that of the specimen described for experiment (*a*).

Alternatively, 21-acetoxy-9α,11β-dichloro-17-hydroxy-16β-methyl-5α-pregnane-3,20-dione (75 g.) in acetic acid (560 ml.) and methylene chloride (188 ml.) containing anhydrous sodium acetate (47 g.) was stirred with acid-washed zinc dust (150 g.) at 55° for 45 min. The zinc was filtered off from the hot solution and washed with a mixture of acetic acid (50 ml.) and methylene chloride (100 ml.). The combined filtrate and washings were evaporated under reduced pressure to remove the methylene chloride, and the product was precipitated by water (560 ml.), filtered off, washed with water, and dried at 100° *in vacuo* giving 61·0 g. (95·7%) of material, m. p. 186—188°, $[\alpha]_D$ +80·5°.

The authors are indebted to Dr. J. E. Page for interpreting the infrared spectra, also to Messrs. H. A. Crisp, R. E. Grigg, and L. A. Wetherill for experimental assistance.

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX. [*Received, April 14th*, 1961.]

895. *Compounds Related to the Steroid Hormones. Part VI.*[1] *The Synthesis of the 9α-Fluoro-16β-methyl Derivatives of Hydrocortisone and Prednisolone.*

By T. R. Carrington, S. Eardley, J. Elks, G. F. H. Green, G. I. Gregory, A. G. Long, and J. C. P. Sly.

Dehydrogenation of 21-acetoxy-17-hydroxy-5α-pregn-9-ene-3,20-dione and its 16β-methyl analogue to the 1,4,9-trienes has been accomplished by a bromination–dehydrobromination sequence. When the double bond of ring c was protected as a 9α,11β-dichloro- or a 9α-bromo-11β-acyloxy-derivative, subsequent dehydrogenation by bromination and dehydrobromination failed owing to rapid elimination of the protecting groups which led to the formation of 7,9-dienes.

21-Acetoxy-9α-fluoro-11β,17-dihydroxypregn-4-ene-3,20-dione and its 16β-methyl analogue were prepared from the corresponding ring-A saturated 9α,11β-fluorohydrins by dibromination, selective dehydrobromination, and subsequent debromination of the 2-bromo-Δ^4-3-ketones. Complete dehydrobromination of the 16-unsubstituted dibromide gave a mixture of 9α-fluoroprednisolone acetate and its $\Delta^{4,6}$-isomer.

Conversion of 5α-pregn-9-en-3-ones such as (VII) (see preceding paper) into the corresponding 1,4,9-trien-3-ones (XVII) by a bromination–dehydrobromination sequence is an important stage in synthesising analogues of steroid hormones from hecogenin *via* intermediates unsaturated at position 9(11). Some initial difficulties were encountered in preparing 2,4-dibromo-5α-pregn-9-en-3-ones (*e.g.*, XV) by brominating the corresponding 3-ketones (VII), and we simultaneously investigated methods of protecting the double bond during dehydrogenation of ring A.

21-Acetoxy-11β,17-dihydroxy-5α-pregnane-3,20-dione was converted [2,3] into the Δ^9-compound (I), which was treated with chlorine (cf. similar reactions with 4,9-dien- and 1,4,9-trien-3-ones [4]) to give 21-acetoxy-9α,11β-dichloro-17-hydroxy-5α-pregnane-3,20-dione (II; X = Y = Cl) in *ca.* 60% yield. Treatment of this dichloride under conditions (see below) used for dehydrohalogenation of 2,4-dibromo-3-oxo-steroids led to ready elimination of two molecules of hydrogen chloride, with formation of a product that appeared from its ultraviolet spectrum (cf. refs. 5, 6, 7) to be a mixture of the 7,9-diene (III) and, probably, the isomeric 8(14),9-diene (IV). On conducting the dehydrochlorination with lithium carbonate and lithium chloride in dimethylacetamide (cf. ref. 8) at 95° and purifying the product by treatment with maleic anhydride to remove the homoannular diene (IV), we were able to isolate 21-acetoxy-17-hydroxy-5α-pregna-7,9-diene-3,20-dione (III). Further experiments showed that 21-acetoxy-9α,11β-dichloro-17-hydroxypregna-1,4-diene-3,20-dione [4] was more stable to dehydrochlorination than was the ring-A saturated compound (II; X = Y = Cl).

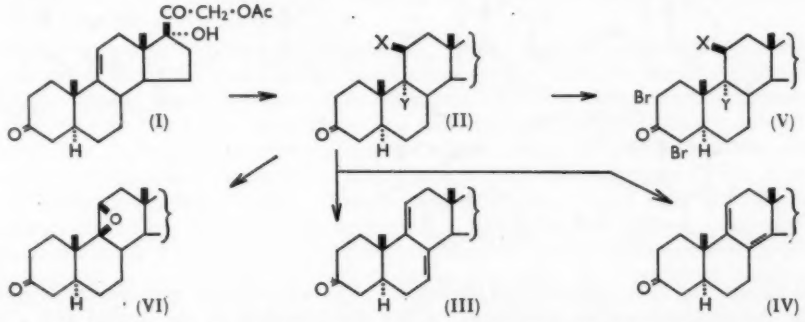
Bromination of the dichloro-compound (II; X = Y = Cl) in acetic acid gave crude 21-acetoxy-2,4-dibromo-9α,11β-dichloro-17-hydroxy-5α-pregnane-3,20-dione (V; X = Y = Cl). Dehydrohalogenation of this material at 55° with dimethylacetamide containing

[1] Part V, preceding paper.
[2] Evans, Green, Hunt, Long, Mooney, and Phillipps, *J.*, 1958, 1529.
[3] Elks, Phillipps, and Wall, *J.*, 1958, 4001.
[4] Robinson, Finckenor, Oliveto, and Gould, *J. Amer. Chem. Soc.*, 1959, **81**, 2191; Reimann, Oliveto, Neri, Eisler, and Perlman, *ibid.*, 1960, **82**, 2308; Robinson, Finckenor, Tiberi, Eisler, Neri, Watnick, Perlman, Holroyd, Charney, and Oliveto, *ibid.*, p. 4611.
[5] Dorfman, *Chem. Rev.*, 1953, **53**, 47; Antonucci, Bernstein, Giancola, and Sax, *J. Org. Chem.*, 1951, **16**, 1891; Heusler and Wettstein, *Helv. Chim. Acta*, 1952, **35**, 284.
[6] Wendler, Graber, Snoddy, and Bollinger, *J. Amer. Chem. Soc.*, 1957, **79**, 4476.
[7] Fried and Sabo, *J. Amer. Chem. Soc.*, 1954, **76**, 1455; 1957, **79**, 1130.
[8] Holysz, *J. Amer. Chem. Soc.*, 1953, **75**, 4432.

calcium carbonate [9] gave bromine-containing products with the characteristic ultraviolet absorption of the 7,9-diene chromophore, but without the infrared absorption attributable to conjugated chromophores in ring A. Similar results were obtained with collidine at 95°.

Dechlorination of the 9α,11β-dichloro-compound (II; X = Y = Cl) to the Δ^9-steroid (I) was effected in high yield by either 2 mol. of chromous chloride [1,4] or hydrogen and palladised charcoal, preferably in the presence of triethylamine.[1] We attempted to prepare 21-acetoxy-2,4-dibromo-17-hydroxy-5α-pregn-9-ene-3,20-dione (*e.g.*, XV; R = H) by selective dechlorination of the 2,4-dibromo-9α,11β-dichloro-compound (V; X = Y = Cl) with 2 mol. of chromous chloride, but obtained only an impure product with infrared absorption attributable to mono-α-bromo-ketones. Hydrogenolysis of the tetrahalide (V; X = Y = Cl) over palladium–charcoal in tetrahydrofuran containing triethylamine gave a mixture of the 9-ene (I) (81%) and the 9α,11β-dichloro-compound (II; X = Y = Cl) (13%). The latter was obtained in 74% yield when hydrogenolysis was carried out in acetic acid.

In another attempt to protect the 9,11-double bond, compound (I) was treated with *N*-bromoacetamide in formic or acetic acid containing, respectively, sodium formate or lithium acetate, to give the corresponding 9α-bromo-11β-acyloxy-derivatives [10,11] (II; Y = Br, X = H·CO_2 and AcO, respectively) in moderate yields. Preliminary experiments in which these derivatives were treated with calcium carbonate in dimethylacetamide at the b. p. or 95—100° afforded the 7,9-diene (III), possibly contaminated with the 8(14),9-diene (IV). In view of the similarity between these products and those obtained by



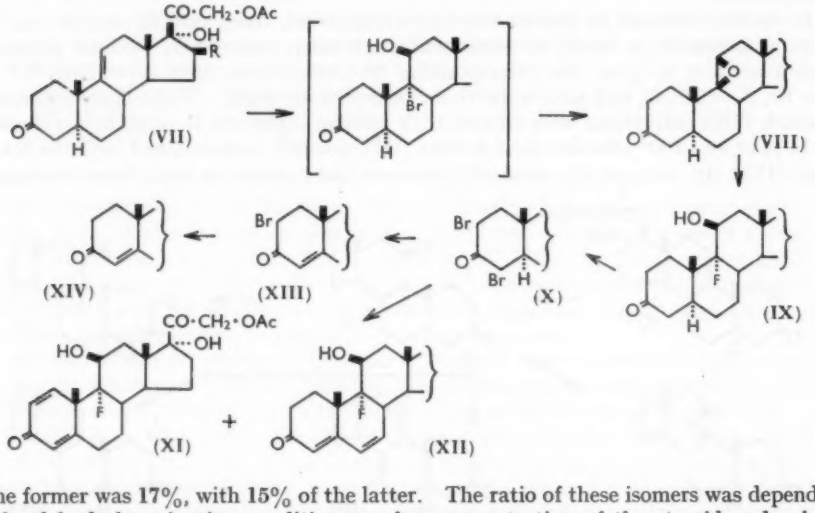
dehydrochlorination of the 9α,11β-dichloro-compound (II; X = Y = Cl), we did not pursue attempts at dehydrobrominating the 11β-acyloxy-2,4,9α-tribromides (V; X = R·CO_2, Y = Br) in ring A.

Treating 21-acetoxy-9α-bromo-11β-formyloxy-17-hydroxy-5α-pregnane-3,20-dione (II; X = H·CO_2, Y = Br) in aqueous dioxan with a solution of sodium hydroxide [10] and reacetylating the product gave a 79% yield of the 9β,11β-epoxide (VI). When, however, we attempted this conversion by refluxing the formate in ethanol containing potassium acetate,[3,7,12] we obtained a mixture of the 7,9-diene (III), the 9β,11β-epoxide (VI), and 21-acetoxy-17-hydroxy-5α-pregnane-3,11,20-trione. The formation of an 11-ketone from 9α-bromo-11β-hydroxyergostan-3-one in similar circumstances has been reported.[3]

Acid-catalysed bromination of the epoxide (VI) led to simultaneous cleavage of the oxiran [13] and bromination of ring A to give the crude tribromide (V; X = OH, Y = Br). Attempts to reform the 9β,11β-epoxide ring, with or without dehydrobromination in ring A, were unsuccessful.

[9] Part II, Green and Long, *J.*, 1961, 2532.
[10] Robinson, Finckenor, Kirtley, Gould, and Oliveto, *J. Amer. Chem. Soc.*, 1959, **81**, 2195.
[11] Levine and Wall, *J. Amer. Chem. Soc.*, 1959, **81**, 2826.
[12] Hirschmann, Miller, Wood, and Jones, *J. Amer. Chem. Soc.*, 1956, **78**, 4956.
[13] Fried and Sabo, *J. Amer. Chem. Soc.*, 1955, **77**, 4181; B.P. 829,632, 829,633.

A route [3,13,14,15] to 9α-fluoroprednisolone acetate (XI) that avoids the necessity for brominating a Δ^9-5α-3-ketone involves conversion of such a compound (VII; R = H) into the corresponding 9α-fluoro-11β-hydroxy-5α-3-ketone (IX; R = H), which is then dehydrogenated *via* the 2,4-dibromo-compound (X; R = H) into the required $\Delta^{1,4}$-3-ketone (XI). This route has previously given poor results, but it seemed to merit reinvestigation, and we therefore studied the complete dehydrobromination of the crude 2,4-dibromide [3] (X; R = H) with calcium carbonate in boiling dimethylacetamide,[9] with the same reagents and lithium bromide, or with collidine and dimethylformamide.[15] We had hoped that the inclusion of a metal carbonate [16] would prevent formation of the 4,6-dienone isolated by previous workers [13,14,15] when the dehydrobromination was carried out in a mixture of collidine and dimethylformamide. However, in each instance the product was a mixture (cf. refs. 13, 14, 15, 17) of 9α-fluoroprednisolone acetate (XI) and the isomeric 4,6-dien-3-one (XII); after separation with Girard's reagent P the best yield



of the former was 17%, with 15% of the latter. The ratio of these isomers was dependent on the dehydrobrominating conditions; a low concentration of the steroid and a large excess of suspended calcium carbonate favoured the formation of the cross-conjugated isomer (XI). Addition of lithium bromide resulted in faster reaction [8] and favoured formation of the 4,6-dien-3-one (XII). At lower temperatures (*e.g.*, 100°) complete dehydrobromination was difficult to achieve.

Further investigation of this dehydrobromination confirmed Fried's report [15] that the second molecule of hydrogen bromide is eliminated much more slowly than the first. Several other instances of selective monodehydrobromination of diequatorial 2,4-dibromo-3-ketones in both the 5α- and the 5β-series have been reported.[16,18,19] By conducting the reaction at 100° with calcium carbonate and lithium bromide in dimethylacetamide, we isolated 21-acetoxy-2-bromo-9α-fluoro-11β,17-dihydroxypregn-4-ene-3,20-dione [15] (XIII; R = H). Debromination with chromous chloride then gave 9α-fluorocortisol acetate [3,7,12]

[14] Hirschmann, Miller, Beyler, Sarett, and Tishler, *J. Amer. Chem. Soc.*, 1955, **77**, 3166; U.S.P. 2,837,541.
[15] Fried, U.S.P. 2,848,464—5.
[16] Joly, Warnant, Nominé, and Bertin, *Bull. Soc. chim. France*, 1958, 366, 367; Joly and Warnant, U.S.P. 2,957,890.
[17] Bernstein, Brown, Feldman, and Rigler, *J. Amer. Chem. Soc.*, 1959, **81**, 4956.
[18] Inhoffen and Zühlsdorff, *Ber.*, 1943, **76**, 233; Djerassi and Scholz, *J. Amer. Chem. Soc.*, 1947, **69**, 2404; *J. Org. Chem.*, 1948, **13**, 697.
[19] Wieland, Heusler, and Wettstein, *Helv. Chim. Acta*, 1960, **43**, 523.

(XIV; R = H) in 43% yield from the dibromide (X; R = H). In the same way the 16β-methyl-fluorohydrin (IX; R = Me), prepared by the usual method from the Δ^9-compound (VII; R = Me), was converted into the corresponding dibromide (X; R = Me); subsequent monodehydrobromination and debromination gave 21-acetoxy-9α-fluoro-11β,17-dihydroxy-16β-methylpregn-4-ene-3,20-dione [20] (XIV; R = Me) in 22% yield. The low yield obtained in the 16β-methyl series compared with that in the unsubstituted series is attributed, at least in part, to a less polar impurity arising during the bromination of the fluorohydrin (IX; R = Me) in glacial acetic acid. A corresponding fraction occurring (paper chromatography) in the subsequent stages was easily removed during crystallisation of the final product and is tentatively considered to be due to loss of the 17-hydroxy-group and formation of a 16-methyl-Δ^{16}-20-ketone. The easy elimination of a 17α-hydroxy-group in the 16β-methyl series compared with elimination in the 16α-methyl or unmethylated series has been commented upon previously.[20]

Meanwhile we had found suitable conditions for bromination of 3-oxo-5α-pregn-9-enes (VII) in ring A. A few such examples have been recorded elsewhere for both 5α- [2,3] and 5β-steroids.[21] We studied the bromination of 21-acetoxy-17-hydroxy-5α-pregn-9-ene-3,20-dione (VII; R = H) in several solvents. The crude 2,4-dibromides [2] were assayed by determining the yield of triene (XVII; R = H) [4,13,14,22] obtained on dehydrobromination under standard conditions. Best yields (*ca.* 40%) were obtained when the bromination was conducted in dioxan–acetic acid (cf. ref. 19). More reliable brominations were achieved by initiating the reaction with hydrogen bromide, presumably because bromination of the 3-ketone is acid-catalysed and therefore favoured over addition of bromine to the ring-c double bond.

Dibromination of the 16β-methyl analogue [1] (VII; R = Me) was best conducted in dioxan, either alone or containing up to an equal volume of acetic acid.[19] Under these conditions two crystalline 2,4-dibromides were isolated, whose debromination regenerated the starting material (VII; R = Me). The more plentiful, dextrorotatory, isomer was assigned the 2α,4α(*eq,eq*)-dibromo-ketone structure (XV; R = Me), and the minor, lævorotatory, component was assigned the 2α,4β(*eq,ax*)-dibromo-structure (XVI; R = Me) on the evidence presented below. French workers [23] have found that bromination of 21-acetoxy-4β-bromo-17-hydroxy-5β-pregnane-3,11,20-trione and related compounds in dioxan leads to the 2α,4β(*ax,eq*)-dibromo-5β-pregnane whereas bromination with *N*-bromosuccinimide in benzyl alcohol gives the 2β,4β(*eq,eq*)-isomer. Acid-catalysed bromination in solvents other than dioxan gave inseparable isomeric mixtures. It is significant that the energies of axial and equatorial forms of some α-bromo-ketones are nearly the same in dioxan solution, whereas they differ much more in other solvents.[24]

The main features distinguishing the infrared spectra [23,25] of dibromides (XV and XVI; R = Me) in bromoform solution are bands, in the former, at 948 (unassigned) and 1745 cm.$^{-1}$, which are absent from the spectrum of the latter. The low-frequency spectrum (potassium bromide prism) in carbon disulphide of the 2α,4α-dibromide (XV; R = Me) showed expected [25] bands at 687 and 614 cm.$^{-1}$, absent from the spectrum of its isomer. Crude bromination products showed absorption at 1745 cm.$^{-1}$, less intense than that of the pure 2α,4α-isomer (XV; R = Me).

Differences in molecular rotation provide some support for the assignment of these structures. Of the four possible types of 2,4-dibromo-3-oxo-5α-steroids, only

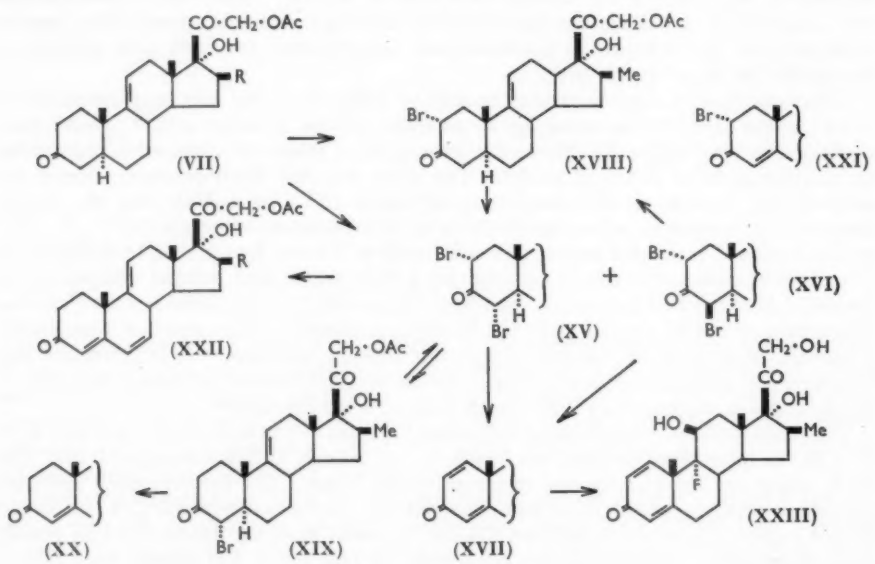
[20] Taub, Hoffsommer, Slates, Kuo, and Wendler, *J. Amer. Chem. Soc.*, 1960, **82**, 4012.
[21] Graber, Haven, and Wendler, *J. Amer. Chem. Soc.*, 1953, **75**, 4722; Casanova, Shoppee, and Summers, *J.*, 1953, 2983.
[22] Hogg, Lincoln, Nathan, Hanze, Schneider, Beal, and Korman, *J. Amer. Chem. Soc.*, 1955, **77**, 4438.
[23] Muller, Joly, Nominé, and Bertin, *Bull. Soc. chim. France*, 1956, 1457; Joly, Nominé, and Bertin, *ibid.*, p. 1459.
[24] Alinger and Alinger, *Tetrahedron*, 1958, **2**, 64; Kumler and Huitric, *J. Amer. Chem. Soc.*, 1956, **78**, 3369.
[25] Cummins and Page, *J.*, 1957, 3847, and refs. therein cited.

the 2α,4α-compounds have been described in the literature. However, the effect of 2,4-dibromination on the molecular rotation of a 3-oxo-5α-steroid can be calculated from the individual effects of 2- and 4-monobromination,[26] if vicinal action is assumed to be absent; rotation differences calculated in this way are presented in the Table.

Br	2α, 4α	2α, 4β	2β, 4α	2β, 4β
$\Delta[M]_D$	−65° to −157°	−338° to −486°	+333° to +477°	+4° to +211°

Some justification for this method is found in the fact that the observed values of $\Delta[M]_D$ for 2α,4α-dibromination of a number of 3-oxo-5α-steroids lie within the range quoted; an 11-oxo-group may introduce anomalies,[27] but, significantly for our present purpose, a 9,11-double bond does not.[2] The observed values of $\Delta[M]_D$ for our 2α,4α- (XV; R = Me) and 2α,4β-dibromo-compounds (XVI; R = Me) in comparison with the parent ketone (VII; R = Me) were −67° and −476°, respectively, both lying within the calculated ranges.

Optical rotatory dispersion measurements show that the 2α,4α-dibromo-ketone (XV; R = Me) gives a positive Cotton effect, whereas with the 2α,4β-isomer (XVI; R = Me) the effect is negative. The shift of the extremum (315 ⟶ 330 mμ) and application of the halogeno-ketone rule [28,29] accord with the proposed structures (XV and XVI; R = Me) provided that ring A is in the chair conformation.



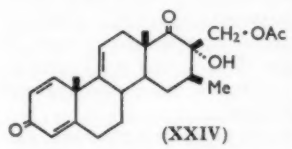
Partial reduction of the 2α,4α- (XV; R = Me) and the 2α,4β-dibromo-ketones (XVI; R = Me) with chromous chloride gave the 4α- [26,27] (XIX) and the 2α-bromo-ketones (XVIII), respectively, the latter also arising on monobromination of the unsubstituted ketone (VII; R = Me). Attention is called to the fact that the axial bromine in the

[26] Malunowicz, Fajkoš, and Šorm, *Coll. Czech. Chem. Comm.*, 1960, **25**, 1359; Fajkoš and Šorm, *ibid.*, 1959, **24**, 3115; Klinot and Vystrčil, *Chem. and Ind.*, 1960, 1360.
[27] Evans, Hamlet, Hunt, Jones, Long, Oughton, Stephenson, Walker, and Wilson, *J.*, 1956, 4356.
[28] Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill, New York, 1960.
[29] Klyne in "Advances in Organic Chemistry, Methods and Results," Interscience Publ., Inc., New York, 1960, Vol. I, pp. 239 *et seq.*

2α,4β-dibromide (XVI; R = Me) was preferentially reduced. Bromination of the 4α-bromo-compound (XIX; R = Me) gave the 2α,4α-dibromide (XV; R = Me), whereas dehydrobromination with semicarbazide base and subsequent treatment with pyruvic acid [27] gave 21-acetoxy-17-hydroxy-16β-methylpregna-4,9-diene-3,20-dione [20] (XX). Partial dehydrobromination of the 2α,4β-dibromide (XVI; R = Me) gave the corresponding 2-bromo-3-oxo-4-ene (XXI; R = Me) (cf. refs. 16, 18, 19) which was not fully purified.

Each of the 2,4-dibromo-3-ketones (XV, XVI; R = Me) gave the triene (XVII; R = Me) [20] on complete dehydrobromination, but rather better overall yields were obtained by using the total crude bromination product. Dehydrobromination could be effected with calcium carbonate in boiling dimethylacetamide,[9] but more reliable results attended the use of these reagents, together with lithium bromide at about 100°. Surprisingly,[16,19] the replacement of calcium carbonate with lithium carbonate was conducive to the formation of the 4,6-dien-3-one (XXII; R = Me). After removal of by-products with Girard's reagent P,[27] 21-acetoxy-17-hydroxy-16β-methylpregna-1,4,9-triene-3,20-dione [20,30] (XVII; R = Me) was obtained in about 50% overall yield from the Δ^9-compound (VII; R = Me).

The crude dehydrobromination products contained, besides the isomeric trienes (XVII and XXII; R = Me), at least one D-homo-compound (*e.g.*, XXIV); an isolated specimen had infrared absorption, optical rotation, and paper-chromatographic characteristics consistent with such a structure (cf. ref. 20). A band at 1810 cm.$^{-1}$ in the infrared spectra of some crude specimens of the triene (XVII; R = Me) was attributed to the carbonyl group in a 17α,21-oxide but we did not isolate a pure compound.



(XXIV)

The 16β-methyl-triene (XVII; R = Me) was converted into 9α-fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione (XXIII) through the 9α,11β-bromohydrin and the 9β,11β-epoxide by methods similar to those reported elsewhere.[20,30]

Experimental

M. p.s were taken on the Kofler block and are uncorrected; " cap." refers to m. p.s (corrected) taken in a capilliary tube. Unless otherwise stated, ultraviolet and infrared spectra were measured for solutions in ethanol and bromoform, respectively. Optical rotations refer to 1·0 ± 0·3% solutions in chloroform at 22° ± 4°; optical rotatory dispersion [31] values are for 0·1% solutions in chloroform. Paper chromatograms were run at 35° on Whatman No. 2 papers with solvent F [32] or propylene glycol and toluene [33] (indicated by the letters F and Z respectively); the components were located with TSTZ spray [32] or reflex photography with an ultraviolet light source. The pure 20-oxo-17α,21-diols and their esters were assayed by the tetrazolium method [34] (with cortisone acetate as standard), the results being within ±5% of the theoretical values. Extracts in organic solvents were dried over magnesium sulphate before evaporation. Chromous chloride was made either by the reduction of the chromic salt [35] or, better, by dissolving 99·999% pure chromium (New Metals and Chemicals Ltd., Chancery Lane, London, W.C.2) in warm, dilute hydrochloric acid (3 mol.) under nitrogen.[36] Calcium carbonate in a suitably fine form was bought as " Calofort U " from J. and E. Sturge Ltd., 1, Whealeys Road, Birmingham. Charcoal (Nuchar G-190, unground) was obtained from the Pulp and Paper Co., 230, Park Avenue, New York 17, U.S.A. Dioxan, purified as described by Vogel,[37] was stored in the frozen state under nitrogen.

[30] Oliveto, Rausser, Herzog, Hershberg, Tolksdorf, Eisler, Perlman, and Pechet, *J. Amer. Chem. Soc.*, 1958, **80**, 6687.
[31] Klyne and Parker in " Technique of Organic Chemistry, Vol. I; Physical Methods of Organic Chemistry, Part III," Interscience Publ., Inc., New York, 1960, pp. 2335 *et seq.*
[32] Brooks, Hunt, Long, and Mooney, *J.*, 1957, 1175.
[33] Neher in " Chromatographic Reviews," Elsevier, Amsterdam, 1959, pp. 141 *et seq.*
[34] Mader and Buck, *Analyt. Chem.*, 1952, **24**, 666.
[35] Rosenkranz, Mancera, Gatica, and Djerassi, *J. Amer. Chem. Soc.*, 1950, **72**, 4077.
[36] Lux and Illmann, *Chem. Ber.*, 1958, **91**, 2143.
[37] Vogel, " Text-Book of Practical Organic Chemistry," Longman, Green and Co., London, 1948, p. 175.

21-Acetoxy-17-hydroxy-5α-pregn-9-ene-3,20-dione (I).—21-Acetoxy-11β,17-dihydroxy-5α-pregnane-3,20-dione was dehydrated as previously described;[2] the product was crystallised from chloroform and dried by refluxing it with toluene in a Dean–Stark apparatus to give the steroid (I), m. p. 243—254° (decomp.), $[\alpha]_D$ +69°. Complete removal of solvent was difficult; a sample sublimed at 180—200° *in vacuo* had m. p. 256—257°, $[\alpha]_D$ +71°. This compound was also prepared in good yield by refluxing the 11β-alcohol in glacial acetic acid containing lithium bromide[38] for 30 minutes.

21-Acetoxy-9α,11β-dichloro-17-hydroxy-5α-pregnane-3,20-dione (II; X = Y = Cl).—(*a*) The Δ^9-compound (I) (0·5 g.) in chloroform (75 ml.) containing pyridine (0·31 ml., 3 mol.) was treated with a solution of chlorine (106 mg., 1·1 mol.) in carbon tetrachloride (3·4 ml.). After 8 min. the mixture was washed successively with dilute sodium thiosulphate, dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water. The chloroform layer yielded a solid which crystallised from acetone to give the *9α,11β-dichloride* (II; X = Y = Cl) (0·38 g., 64%), m. p. 205—209° (decomp.), $[\alpha]_D$ +84°, $\nu_{max.}$ 1744 and 1230 (21-OAc), 1725 (20-C=O) and 1705 cm.$^{-1}$ (3-C=O) (Found: C, 60·0; H, 6·9; Cl, 15·3. $C_{23}H_{32}Cl_2O_5$ requires C, 60·1; H, 7·0; Cl, 15·4%). Attempts to crystallise this material from methanol resulted in degradation to products containing the 7,9-diene chromophore.

(*b*) To a stirred suspension of the Δ^9-compound (I) (10·0 g.) in acetic acid (600 ml.) containing anhydrous lithium chloride (60 g.) was added *N*-chlorosuccinimide (4·0 g.; 94% active halogen) and anhydrous hydrogen chloride (1·2 g.) in tetrahydrofuran (12 ml.). Complete solution was achieved in 10 min.; after a total of 1 hr. the solution was poured into water, and the product was crystallised from acetone, giving the dichloride (II; X = Y = Cl) (6·0 g., 51%), m. p. 207—210° (decomp.), $[\alpha]_D$ +84°. The mother-liquors, treated under nitrogen with chromous chloride, gave the Δ^9-compound (I) (1·5 g.), m. p. 238—240°.

Dehydrochlorination of 21-Acetoxy-9α,11β-dichloro-17-hydroxy-5α-pregnane-3,20-dione (II; X = Y = Cl).—The dichloride (4·0 g.) was added to a stirred suspension of lithium chloride (1·5 g.) and lithium carbonate (4·8 g.) in dimethylacetamide (60 ml.) at 95°. After 20 min. the mixture was poured into an excess of dilute hydrochloric acid and the steroid (3·9 g.), $\lambda_{max.}$ ($E^{1\%}_{1\,cm.}$) at 235 (244), 242 (269), 250 (186), and 271 mμ (26), was isolated with methylene chloride. This material was refluxed for 5 hr. in toluene (150 ml.) containing maleic anhydride (1·5 g.). The resulting crystals were recrystallised twice from ethanol and dried azeotropically with xylene, giving the *7,9-diene* (III), m. p. 228—230°, $[\alpha]_D$ +87°, $\lambda_{max.}$ 234·5 (ε 14,900), 241·5 (ε 16,200), and 250 mμ (ε 10,900), $\nu_{max.}$ 1745 and 1240 (21-OAc), 1728 (20-C=O) and 1708 cm.$^{-1}$ (3-C=O). Despite extensive drying the analysis was not very satisfactory and infrared spectra showed traces of moisture (Found: C, 70·9; H, 7·8. $C_{23}H_{30}O_5$ requires C, 71·5; H, 7·8%).

Similar crude dehydrochlorination products were obtained when the dichloride (II; X = Y = Cl) was treated with calcium carbonate in dimethylacetamide at the b. p., 95°, and 55°, whereas no reaction was apparent at room temperature over a period of 18 hr. Rapid dehydrochlorination also occurred in boiling collidine. In comparison with these results the cross-conjugated ketone 21-acetoxy-9α,11β-dichloro-17-hydroxypregna-1,4-diene-3,20-dione was unchanged by being heated at 55° or at 95° for 6 hr. in dimethylacetamide containing calcium carbonate.

21-Acetoxy-2,4-dibromo-9α,11β-dichloro-17-hydroxy-5α-pregnane-3,20-dione (V; X = Y = Cl).—The dichloride (II; X = Y = Cl) (1·0 g.) in acetic acid (90 ml.) was treated with a solution of bromine (770 mg., 2·1 mol.) in acetic acid (11 ml.). The optical rotation of the mixture reached a steady value in 16 hr. Dilution with water gave crude 2,4-dibromo-9α,11β-dichloride (V; X = Y = Cl), m. p. 141—143°, $[\alpha]_D$ +56° (Found: halogen, 38·4. Calc. for $C_{23}H_{30}Br_2Cl_2O_5$: halogen, 37·4%), which was not purified.

Dehydrohalogenation of this material resulted in preferential elimination of hydrogen chloride.

Dehalogenation of 21-Acetoxy-9α,11β-dichloro-17-hydroxy-5α-pregnane-3,20-dione (II; X = Y = Cl).—(a) *With chromous chloride.* The dichloride (0·17 g.) in acetone (40 ml.) consumed 1·97 equiv. of M-chromous chloride (5 ml.) in 30 min. at room temperature, to give the Δ^9-compound (I), m. p. 235—247°.

(b) *By hydrogenation.* The dichloride (II; X = Y = Cl) (0·46 g., 1 mmole) in tetrahydrofuran (40 ml.) containing triethylamine (0·42 ml., 3 mmoles) was hydrogenated in the presence

[38] Herz and Fried, U.S.P. 2,842,568.

of pre-reduced 10% palladium–charcoal (0·10 g.). After 18 min. hydrogen uptake was complete and the Δ^9-compound (I) (0·38 g.), m. p. 241—244°, was isolated; crystallisation from chloroform raised the m. p. to 253—257°.

Dehalogenation of the Tetrahalide (V; X = Y = Cl).—(a) *With chromous chloride.* Reduction of the tetrahalide with chromous chloride in acetone or acetic acid was conducted at −30°, 0°, or room temperature. The products contained bromine and chlorine and showed infrared absorption at 1725 cm.$^{-1}$ attributed to α-monobromo-ketones. No pure compound was isolated.

(b) *By hydrogenation.* The tetrahalide (V; X = Y = Cl) (0·5 g.) in acetic acid (50 ml.) was hydrogenated in the presence of pre-reduced 10% palladium–charcoal (50 mg.). The product, isolated after the uptake of 2 mol. of hydrogen, was proved by mixed m. p. and infrared spectra to be the dichloride (II; X = Y = Cl) (0·28 g., 74%). Hydrogenation in tetrahydrofuran containing triethylamine (4 equiv.) gave the 9-ene (I) (81%) and the dichloride (II; X = Y = Cl) (13%).

21-*Acetoxy*-9α-*bromo*-11β-*formoxy*-17-*hydroxy*-5α-*pregnane*-3,20-*dione* (II; X = H·CO_2, Y = Br).—A stirred suspension of 21-acetoxy-17-hydroxy-5α-pregn-9-ene-3,20-dione (I) (5·0 g.) and sodium formate (20 g.) in 98% formic acid (50 ml.) was treated under nitrogen with *N*-bromosuccinimide (2·0 g.) during 1 hr. Then the clear solution was stirred for 2 hr. The product (5·35 g.), isolated by dilution with water (1 l.), crystallised from ether–acetone to give the 9α-*bromo*-11β-*formate* (4·6 g., 70%), m. p. 152—157°. A specimen dried at 80° *in vacuo* had m. p. 159—161°, $[\alpha]_D$ +99°, $\nu_{max.}$ 1745 and 1236 (21-OAc), 1722 (20-C=O), and 1714 cm.$^{-1}$ (11β-formate) (Found: C, 55·6; H, 6·7; Br, 15·6. $C_{24}H_{33}BrO_7$ requires C, 56·1; H, 6·5; Br, 15·6%).

11β,21-*Diacetoxy*-9α-*bromo*-17-*hydroxy*-5α-*pregnane*-3,20-*dione* (II; X = OAc, Y = Br).—When a similar preparation to the last was carried out with lithium acetate (20 g.) in acetic acid (250 ml.) the diacetate (4·1 g., 61%) was obtained with m. p. 135—137°, $[\alpha]_D$ +102°, $\nu_{max.}$ 1740 and 1235 (21-OAc), 1725 and 1250 (11β-OAc), 1725 (20-C=O), and 1705 cm.$^{-1}$ (3-C=O). This compound could not be freed from traces of solvent and water and a satisfactory analysis was not obtained. These products gradually darkened to a deep purple when left at room temperature for several weeks.

Stability of the 9α-*Bromo*-11β-*acylates to Dehydrobrominating Conditions.*—The formate (II; X = H·CO_2, Y = Br) (0·25 g.) was added to a stirred suspension of calcium carbonate (0·25 g.) in dimethylacetamide (10 ml.) at *ca.* 95°. Aliquot parts taken after 5, 10, and 20 min. showed ultraviolet, infrared, and paper-chromatographic characteristics (Z) consistent with those of the 7,9-diene (III). A similar result was obtained by treating the diacetate (II; X = OAc, Y = Br) with calcium carbonate in refluxing dimethylacetamide for 5 min.

21-*Acetoxy*-9β,11β-*epoxy*-17-*hydroxy*-5α-*pregnane*-3,20-*dione* (VI) *from the* 9α-*Bromo*-11β-*formate* (II; X = H·CO_2, Y = Br).—The bromo-formate (5 g.) in dioxan (200 ml.) and water (50 ml.) was stirred under nitrogen and treated with 2N-sodium hydroxide (15 ml.) during 20 min. at such a rate that the pH did not rise above 10. Water (100 ml.) was added during the reaction to maintain a one-phase mixture. After adjustment of the pH to *ca.* 6 the solution was evaporated to a slurry (50 ml.) and diluted with water, to give a white solid (3·2 g.). Acetylation with acetic anhydride in pyridine on the steam-bath for 30 min. and crystallisation of the product from ethyl acetate gave the 9β,11β-epoxide (VI) (2·8 g., 71%), m. p. 214—217°, $[\alpha]_D$ +71°, further identified by comparison of its infrared spectrum with that of authentic material.[3] The mother-liquors yielded a second crop (0·3 g., 8%), m. p. 210—215°.

Treatment of 21-*Acetoxy*-9α-*bromo*-11β-*formoxy*-17-*hydroxy*-5α-*pregnane*-3,20-*dione* (II; X = H·CO_2, Y = Br) *with Potassium Acetate in Ethanol.*—The formate (5 g.) was added to anhydrous potassium acetate (20 g.) in boiling absolute ethanol (500 ml.). After 2 hr. the mixture was concentrated to *ca.* 60 ml. and poured into water (1 l.). The oily product, isolated with methylene chloride, was treated with acetic anhydride in pyridine for 30 min. on a steam-bath. A part (2·0 g.) of the isolated material (3·2 g.) in benzene (40 ml.) was separated into its components by chromatography on Florisil (60 g.). Individual fractions were submitted to paper chromatography (Z); combination of appropriate fractions and crystallisation gave three compounds (characterised by their ultraviolet, infrared, and paper-chromatographic behaviour): (*a*) the 7,9-diene (III) (0·31 g.), m. p. 223—226°, $[\alpha]_D$ +79° (*c* 0·31), (*b*) the 9β,11β-epoxide (VI) (0·22 g.), m. p. 208—211°, $[\alpha]_D$ +72° (*c* 0·61), and (*c*) 21-acetoxy-17-hydroxy-5α-pregnane-3,11,20-trione [23] (0·12 g.), m. p. 225—232°, $[\alpha]_D$ +105° (*c* 0·67).

XUM

21-*Acetoxy*-9β,11β-*epoxy*-17-*hydroxy*-16β-*methyl*-5α-*pregnane*-3,20-*dione* (VIII; R = Me).—A stirred suspension of 21-acetoxy-17-hydroxy-16β-methyl-5α-pregn-9-ene-3,20-dione [1] (VII; R = Me) (25 g.) in dioxan (1 l.) containing 0·46N-perchloric acid (100 ml.) was treated in the dark and in a nitrogen atmosphere with *N*-bromoacetamide (11·2 g., 1·3 mol.) at room temperature during 15 min. Thereafter the mixture was stirred for 20 min. The solution was treated with aqueous sodium pyrosulphite until a negative starch–iodide test was obtained. 2N-Sodium hydroxide (95 ml.) was added in 10 min. to bring the pH of the solution to *ca.* 10; during this period it was necessary to add water (600 ml.) to maintain a one-phase solution. After a further 20 min. the pH was adjusted to *ca.* 6 with acetic acid and the solution was concentrated *in vacuo* to 800 ml. Extraction with chloroform and ethyl acetate led to isolation of crude 9β,11β-epoxy-17,21-dihydroxy-16β-methyl-5α-pregnane-3,20-dione as a yellow solid (26 g.). Acetylation with acetic anhydride in pyridine for 30 min. on the steam-bath and crystallisation of the ester from ethanol gave the *acetoxy*-9β,11β-*epoxide* (VIII; R = Me) (20·8 g., 80%), m. p. 209—214° raised by further crystallisation to 213—217°, $[\alpha]_D$ +97°, $\nu_{max.}$ 1742 and 1235 (21-OAc), 1728 (20-C=O), and 1708 cm.$^{-1}$ (3-C=O) (Found: C, 69·2; H, 8·1. $C_{24}H_{34}O_6$ requires C, 68·9; H, 8·2%).

21-*Acetoxy*-9α-*fluoro*-11β,17-*dihydroxy*-16β-*methyl*-5α-*pregnane*-3,20-*dione* (IX; R = Me).—The epoxide (VIII; R = Me) (10·0 g.) in chloroform (150 ml.) was cooled to −30° and added to a similarly cooled solution (60 ml.; 32·2% w/v) of hydrogen fluoride in tetrahydrofuran in a Polythene bottle. The mixture was stirred with a Polythene-coated magnetic stirrer and allowed to warm to 0° in 45 min. Thereafter the temperature was maintained at 0—5° for 5 hr. The mixture was poured into a solution of potassium carbonate (70 g.) in ice-water. Extraction with chloroform led to a crude product (10·6 g.), and three crystallisations from benzene gave the 16β-*methyl*-*fluorohydrin* (IX; R = Me) (4·7 g., 45%), m. p. 215—219°, $[\alpha]_D$ +75°, $\nu_{max.}$ 1744 and 1236 (21-OAc), 1728 (20-C=O) and 1708 cm.$^{-1}$ (3-C=O) (Found: C, 66·0; H, 8·0. $C_{24}H_{35}FO_6$ requires C, 65·7; H, 8·0%).

21-*Acetoxy*-2,4-*dibromo*-9α-*fluoro*-11β,17-*dihydroxy*-16β-*methyl*-5α-*pregnane*-3,20-*dione* (X; R = Me).—(a) *In acetic acid.* The fluorohydrin (IX; R = Me) (1·6 g.) in acetic acid (40 ml.) was treated successively with 6·6N-hydrogen bromide in acetic acid (1·6 ml.) and a solution of bromine (1·23 g., 2·1 mol.) in acetic acid (4·5 ml.). Mutarotation ceased within 40 min. Dilution with water gave the crude 2,4-dibromide (X; R = Me) (1·8 g., 83%), $[\alpha]_D$ +38°, $\lambda_{max.}$ 250 mμ ($E^{1\%}_{1\,cm.}$ 19·2), R_F 0·30 (strong) and 0·70 (weak) (Z). (b) *In dioxan.* In a similar manner the fluorohydrin (IX; R = Me) (2·0 g.) in dioxan (50 ml.) containing 0·6N-hydrogen bromide in acetic acid (2 ml.) was treated with bromine (1·47 g.). After 30 min. the crude dibromide (2·5 g., 92%), $[\alpha]_D$ +44°, was isolated. This product showed no excessive ultraviolet absorption at 250 mμ.

Selective Dehydrobromination of the Dibromide (X; R = Me).—The dibromide (X; R = Me) (1·7 g.; from a bromination in acetic acid) was added to a vigorously stirred suspension of calcium carbonate (1·1 g.) and anhydrous lithium bromide (0·8 g.) in dimethylacetamide (17 ml.) kept at 100° under nitrogen. After 1 hr. the cooled mixture was poured into an excess of dilute hydrochloric acid, to give a solid (1·2 g.). Chromatography on Florisil (30 g.) gave the crude monobromide as a foam (XIII; R = Me) (0·55 g.), $[\alpha]_D$ +128°, $\lambda_{max.}$ 241 mμ ($E^{1\%}_{1\,cm.}$ 268), $\nu_{max.}$ 1742 and 1238 (21-OAc), 1728 (20-C=O) and 1680 cm.$^{-1}$ (2-bromo-Δ^4-3-ketone), R_F 0·24 (strong) and 0·65 (weak) (Z) (Found: Br, 14·9. Calc. for $C_{24}H_{33}BrFO_6$: Br, 15·5%), which was not purified. A similar material, but showing only one spot (R_F 0·25) on paper chromatography was isolated from the crude dibromide (X; R = Me) obtained by bromination in dioxan.

21-*Acetoxy*-9α-*fluoro*-11β,17-*dihydroxy*-16β-*methylpregn*-4-*ene*-3,20-*dione* (XIV; R = Me).—A stirred solution of the 2-bromo-Δ^4-3-ketone (XIII; R = Me) (0·52 g.) in acetone (35 ml.) was debrominated, under nitrogen, with 2·3M-chromous chloride (3 ml.), during 30 min. Isolation with chloroform gave an off-white solid (0·42 g.), $[\alpha]_D$ +135°, $\lambda_{max.}$ 238·5 mμ (ε 15,000), R_F 0·1 (strong), 0·46 (weak) (Z). Two crystallisations from ethyl acetate gave pure 21-*acetoxy*-9α-*fluoro*-11β-17-*dihydroxy*-16β-*methylpregn*-4-*ene*-3,20-*dione* (XIV; R = Me) [0·25 g., 22% based on the dibromide (X; R = Me)], m. p. 223—226° with sintering from 212°, $[\alpha]_D$ +154°, (Found: C, 66·3; H, 7·6. $C_{24}H_{33}FO_6$ requires C, 66·0; H, 7·6%), $\lambda_{max.}$ 238 mμ (ε 16,600), $\nu_{max.}$ 3620 (OH), 1742, and 1238 (21-OAc), 1728 (20-C=O), and 1662 cm.$^{-1}$ (Δ^4-3-C=O), $\nu_{max.}$ (in Nujol) 1740 and 1248 (21-OAc), 1726 (20-C=O), 1664 and 860 cm.$^{-1}$ (Δ^4-3-C=O), R_F 0·10 (Z). Further crystallisation from acetone–hexane gave a polymorphic form [cf. the fluorohydrin (XIV;

R = H)], m. p. 202—206°, $[\alpha]_D$ +153°, $\lambda_{max.}$ 238 mμ (ε 16,800). Taub *et al.*[20] give m. p. 215—225°, $[\alpha]_D$ +170°, $\lambda_{max.}$ 238 mμ (ε 16,800) in MeOH.

Conversion of 21-*Acetoxy*-17-*hydroxy*-5α-*pregn*-9-*ene*-3,20-*dione* (VII; R = H) *into the Fluorohydrin* (XIV; R = H).—The route used for this conversion was that described above for the 16β-methyl series. The Δ^9-steroid (VII; R = H) was converted into the saturated fluorohydrin (IX; R = H), m. p. 227—233°, $[\alpha]_D$ +65°, as previously described.[3] Bromination in acetic acid for 15 min. as described above for the 16β-methyl analogue gave a crude dibromide (X; R = H) (93%) that showed no ultraviolet absorption at *ca.* 250 mμ and only showed one spot on a paper chromatogram (Z). Selective dehydrobromination gave the 2-bromo-Δ^4-compound (XIII; R = H) which crystallised from acetone–hexane as prisms, m. p. 155—168° (decomp.), $[\alpha]_D$ +155°, $\lambda_{max.}$ 240 mμ (ε 15,600), $\nu_{max.}$ 1742 and 1240 (21-OAc), 1730 (20-C=O) 1680, 1630 and 865 cm.$^{-1}$ (2-bromo-Δ^4-3-ketone) (Found: C, 54·8; H, 6·1. Calc. for $C_{23}H_{30}BrFO_6$: C, 55·1; H, 6·0%). Fried [15] reports m. p. 174—175°, $[\alpha]_D$ +136°, $\lambda_{max.}$ 242 mμ (ε 12,200). Debromination of this material with chromous chloride gave 21-acetoxy-9α-fluoro-11β,17-dihydroxypregn-4-ene-3,20-dione [3,7,12] (XIV; R = H), m. p. 208—212° and 231—233° (polymorphic change), $[\alpha]_D$ +149°, $\lambda_{max.}$ 237·5 mμ (ε 16,300), in 43% yield based on the dibromide (X; R = H).

Complete Dehydrobromination of the Dibromide (X; R = H).—The crude dibromide (X; R = H) (1·37 g.) was added to a stirred suspension of calcium carbonate (0·7 g.) in boiling dimethylacetamide (48 ml.). After 80 min. the mixture was cooled and the crude product was isolated by pouring the whole into dilute hydrochloric acid; it (0·98 g.) had $\lambda_{max.}$ ($E^{1\%}_{1\,cm.}$) 241·5 (230) and 276 mμ (250). This material (0·96 g.) in ethanol (15 ml.) containing acetic acid (1·5 ml.) was boiled for 30 min. with Girard's reagent P (0·5 g.). The cooled mixture was poured into sodium hydrogen carbonate solution (150 ml.) and the unchanged material was isolated with ethyl acetate, purified by chromatography on Florisil (5 g.), and crystallised from ethyl acetate, to give the $\Delta^{1,4}$-3-ketone (XI) (0·17 g., 17%), m. p. 230—244° raised by a further crystallisation to 242—247°, $[\alpha]_D$ +103·5° (in acetone), $\lambda_{max.}$ 237·5 mμ (ε 15,600), further identified by comparison of its infrared spectrum with that of authentic material.[3,13,15]

The material forming a Girard's P derivative was regenerated by acidifying the aqueous layer to pH ~ 1 with hydrochloric acid. Isolation and purification as described above gave the $\Delta^{4,6}$-3-ketone (XII) (0·15 g., 15%), m. p. 212—216°, $[\alpha]_D$ +135°, $\lambda_{max.}$ 280 mμ (ε 23,900), $\nu_{max.}$ 1745 and 1235 (21-OAc), 1728 (20-C=O), 1655 and 880 cm.$^{-1}$ ($\Delta^{4,6}$-3-C=O) (Found: C, 65·3; H, 7·0. Calc. for $C_{23}H_{29}FO_6$: C, 65·7; H, 7·0%). For this compound Fried *et al.*[13,15] report m. p. 216—217°, $[\alpha]_D$ +135°, $\lambda_{max.}$ 281 mμ (ε 23,000); Hirschmann *et al.*[14] give m. p. 208°, $[\alpha]_D$ +106° (in acetone), $\lambda_{max.}$ 281 mμ (ε 25,100).

A similar dehydrobromination in which the steroid concentration was 3·2 times as great gave a crude product containing ~70% (ultraviolet and infrared spectra) of the $\Delta^{4,6}$-diene (XII). The addition of anhydrous lithium bromide to the dehydrobromination reaction increased the rate of reaction and also gave mixtures containing a high proportion of the $\Delta^{4,6}$-isomer (XII).

21-*Acetoxy*-17-*hydroxypregna*-1,4,9-*triene*-3,20-*dione* (XVII; R = H).—(a) *From the* Δ^9-*compound* (VII; R = H). A stirred suspension of the Δ^9-steroid (1·0 g.; rubbed through a 100-mesh sieve) in pure dioxan (100 ml.) containing 6·6N-hydrogen bromide in acetic acid (1·66 ml.) was treated (2 min.) with a 1·26N-solution of bromine in acetic acid (8·17 ml., 2·0 mol.). The steroid dissolved during the next 6 min. and after a total of 20 min. the mixture was poured into 15% sodium acetate solution (750 ml.). The crude dibromo-steroid was isolated as a white powder by extraction into ether and removal of solvent *in vacuo* at <25°; last traces of dioxan were eliminated by freeze-drying.

An intimate mixture of this material with calcium carbonate (0·75 g.) was added to a stirred suspension of calcium carbonate (0·75 g.) in refluxing dimethylacetamide (15 ml.) under nitrogen. After 15 min. the mixture was cooled and poured into ice-cold 2N-hydrochloric acid (200 ml.). Extraction with ethyl acetate led to a brown solid (0·93 g.) that was boiled for 15 min. in ethanol (30 ml.) containing acetic acid (0·9 ml.) and Girard's reagent P (0·6 g.). The portion that failed to form a water-soluble derivative was isolated with chloroform, dissolved in benzene, and purified on a column of charcoal, the fractions being tested by paper chromatography. Combination of appropriate fractions (0·56 g.) and crystallisation from acetone–light petroleum (b. p. 60—80°) (1 : 5) gave the triene (XVII; R = H) (0·41 g., 42%), m. p. 221—226°, $[\alpha]_D$ +54° (*c* 0·38), $\lambda_{max.}$ 237·5 mμ (ε 14,700).

XUM

Use of chloroform, acetic acid, or tetrahydrofuran as solvents for the bromination resulted in isolation of the triene (XVII; R = H) in 33, 28, and 26% yield respectively. In the case of chloroform there was evidence of uptake of bromine from hydrogen bromide alone.

(b) *By dehydration of* 21-*acetoxy*-11β,17-*dihydroxypregna*-1,4-*diene*-3,20-*dione*. A solution of prednisolone acetate [39] (40 g.) in dry pyridine (600 ml.) at *ca.* −25° was added, with stirring and under nitrogen, to a mixture of freshly distilled thionyl chloride (16 ml.) in dry pyridine (600 ml.) prepared and maintained at *ca.* −25°. After 45 min. at this temperature the reaction mixture was poured with stirring into ice and dilute hydrochloric acid. After 1 hr. the solid was collected, washed with water, and dried *in vacuo* [37·5 g., 98%; R_F 0·73, and 0·92 (weak) (F)]. The fast-running impurity remains unidentified.

The product was purified by dissolving it in boiling ethanol (2·5 l.) and ethyl acetate (300 ml.) and adding a solution of sodium pyrosulphite (250 g.) in water (500 ml.). The resulting suspension was boiled for 4 hr., cooled, and poured into 10% sodium pyrosulphite (10 l.). The solid was collected, dried, and crystallised from ethyl acetate, to give the triene (XVII; R = H) (27·8 g., 73%), m. p. 224—227°, $[\alpha]_D$ +54°, R_F 0·73 (F), $\lambda_{max.}$ 237·5 mμ (ε 15,700), $\nu_{max.}$ 1743, and 1235 (21-OAc), 1725 (20-C=O), 1658, and 888 cm.$^{-1}$ ($\Delta^{1,4}$-3-C=O). Hogg *et al.*[22] give m. p. 223—226°, $[\alpha]_D$ +75°; however, constants quoted elsewhere [4,7] are in good agreement with ours.

21-*Acetoxy*-2α,4α-*dibromo*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*ene*-3,20-*dione* (XV; R = Me).—(*a*) The Δ^9-compound (VII; R = Me) (10 g.) was suspended in dioxan (125 ml.) and acetic acid (125 ml.) and stirred under nitrogen. Successive additions of 0·6N-hydrogen bromide in acetic acid (9·0 ml.) and 0·94M-bromine in acetic acid (56·0 ml., 2·0 mol.) were completed in 4 min. The pale yellow solution was stirred for a total of 22 min. to allow for completion of mutarotation. The solid, obtained by pouring the mixture into sodium acetate in ice-water, was extracted with ether, washed with aqueous sodium hydrogen carbonate, dried, and recovered at <30°. Crystallisation of the product from a mixture of ethyl acetate (120 ml.) and hexane (500 ml.) gave the 2α,4α-*dibromide* (XV; R = Me) as needles (6·45 g., 47%), m. p. 201—203° (cap.; corr.) with decomposition, $[\alpha]_D$ +45°, R.D. [α] (*318* mμ) +1430°, $\nu_{max.}$ 1745 (2α,4α-dibromo-3-ketone), 1745 and 1236 (21-OAc), and 1728 cm.$^{-1}$ (20-C=O) (Found: C, 51·2; H, 5·8; Br, 29·0. $C_{24}H_{32}Br_2O_5$ requires C, 51·5; H, 5·8; Br, 28·5%).

During one experiment the crude dibromide, isolated by extraction with methylene chloride, darkened and partly decomposed when left at *ca.* 5° overnight. During recovery of starting material (VII; R = Me) by hydrogenolytic debromination we also isolated a small amount of 21-*acetoxy*-16β-*methyl*-5α-*pregna*-9,16-*diene*-3,20-*dione* as birefringent plates, m. p. 174—181°, $[\alpha]_D$ +77° (*c* 0·52), $\lambda_{max.}$ 251 mμ (ε 8200), $\nu_{max.}$ 1744 and 1230 (21-OAc), 1706 (3-C=O), 1668, and 1600 (16-methyl-Δ^{16}-20-ketone) (Found: C, 75·2; H, 8·4. $C_{24}H_{32}O_4$ requires C, 75·0; H, 8·4%).

(*b*) *From* 21-*acetoxy*-4α-*bromo*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*ene*-3,20-*dione* (XIX).—The 4α-bromide (XIX) (2·0 g.) in dioxan–acetic acid was treated with hydrogen bromide and bromine (1·05 mol.) for 6 min. as described above; it gave the 2α,4α-dibromide (XV; R = Me) (1·66 g., 71%), m. p. 192—200° (decomp.), $[\alpha]_D$ +49° (Found: Br, 28·9%).

21-*Acetoxy*-2α,4β-*dibromo*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*ene*-3,20-*dione* (XVI; R = Me).—The mother-liquors from the crystallisation of the 2α,4α-dibromide described in (*a*) above were evaporated and the resulting solid was thrice crystallised from ether, giving white needles, m. p. 120—126°, $[\alpha]_D$ −22°. Two crystallisations from acetone gave the 2α,4β-*dibromide* (XVI; R = Me), m. p. 188° (decomp., softening from 170°), $[\alpha]_D^{23}$ −26°, R.D. [α] (*330* mμ), −705°, (*295*), +645°, $\nu_{max.}$ 1740, 1236 (21-OAc), 1740 (2α,4β-dibromo-3-ketone), 1728 cm.$^{-1}$ (20-C=O) (Found: C, 51·3; H, 5·7; Br, 29·0. $C_{24}H_{32}Br_2O_5$ requires C, 51·5; H, 5·8; Br, 28·5%).

Debromination of the Dibromides (XV and XVI; R = Me).—Hydrogenation of the 2α,4α-dibromide (0·50 g.) in 1 : 1 acetic acid–ethyl acetate (50 ml.) containing N-potassium acetate in acetic acid (2·75 ml.) over pre-reduced 5% palladium–carbon, gave the Δ^9-compound (VII; R = Me) (identified by mixed m. p. and infrared spectra) in 78% yield. Similarly, debromination of the 2α,4β-dibromide was accomplished in 79% yield.

21-*Acetoxy*-4α-*bromo*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*ene*-3,20-*dione* (XIX).—The 2α,4α-dibromide (XV; R = Me) (2·0 g.) in acetone (100 ml.) was stirred at −45° under nitrogen while 0·99M-chromous chloride (7·2 ml., 2·0 mol.) was added dropwise. The mixture was allowed to warm to 10° in 35 min., then most of the acetone was removed *in vacuo*. Addition of water and crystallisation of the resulting white solid (1·71 g.) from ethyl acetate gave the

[39] Herzog, Payne, Jevnik, Gould, Shapiro, Oliveto, and Hershberg, *J. Amer. Chem. Soc.*, 1955, **77**, 4781.

4α-bromide (XIX) (0·77 g., 45%) as prisms, m. p. 186—191° (decomp.), $[\alpha]_D$ +34°, R.D. [α] (*313* mμ), +1240°, (*270*), −1500°, $\nu_{max.}$ 1742, and 1235 (21-OAc) and 1725 cm.$^{-1}$ (20-C=O and 4α-bromo-3-ketone) (Found: C, 60·2; H, 7·0; Br, 16·3. $C_{24}H_{33}BrO_5$ requires C, 59·9; H, 6·9; Br, 16·6%).

21-Acetoxy-2α-bromo-17-hydroxy-16β-methyl-5α-pregn-9-ene-3,20-dione (XVIII).—(a) *By bromination of the 9-ene* (VII; R = Me). The ketone (VII; R = Me) (2·0 g.) was dissolved in acetic acid (120 ml.) with warming; the cooled (26°) solution was treated under nitrogen with 0·24M-bromine in acetic acid (24·7 ml., 1·2 mol.) during 5 min. After a total of 15 min. an excess of sodium acetate solution (300 ml.) was added, and the resulting white solid (2·1 g.), $[\alpha]_D$ +89°, was crystallised three times from aqueous acetone, giving prisms of the *2α-bromide* (XVIII), m. p. 211—212° (decomp.), $[\alpha]_D$ +93°, R.D. [α] (*313* mμ), +1740°, $\nu_{max.}$ 1745, 1236 (21-OAc), 1730 (20-C=O and 2α-bromo-3-ketone) (Found: C, 59·6; H, 6·9; Br, 16·8%).

(b) *By debromination of the 2α,4β-dibromide* (XVI; R = Me). A stirred solution of the 2α,4β-dibromide (1·0 g.) in acetone (50 ml.) at −45° under carbon dioxide was treated with 1·06M-chromous chloride (3·4 ml., 2·0 mol.). The mixture warmed to 10° in 26 min.; the acetone was removed *in vacuo* and water was added to precipitate a white solid (0·83 g.), $[\alpha]_D$ +74°. Two crystallisations from aqueous acetone gave the 2α-bromo-ketone (XVIII) (0·58 g., 68%), m. p. 208—211°, $[\alpha]_D$ +92°, identified by infrared spectra with the specimen described above.

21-Acetoxy-17-hydroxy-16β-methylpregna-4,9-diene-3,20-dione (XX).—The 4α-bromide (XIX) (1·0 g.) and finely powdered semicarbazide (0·4 g.) were stirred in a mixture of t-butyl alcohol (80 ml.) and methylene chloride (40 ml.) under carbon dioxide until the solution was colourless (3 hr.).[27] Isolation by standard means gave a halogen-free (Beilstein test) white solid (0·95 g.), $\lambda_{max.}$ 270·5 mμ ($E^{1\%}_{1\,cm.}$ 601). This material in acetic acid (30 ml.) was heated with redistilled pyruvic acid (0·58 ml., 4 mol.) and water (10 ml.) on a steam-bath for 30 min. The crystalline product, dissolved in methylene chloride, was washed with sodium hydrogen carbonate solution and dried. Three crystallisations of the product from ethanol gave plates of the 4,9-diene (XX), m. p. 213—215°, $[\alpha]_D$ +130°, $\lambda_{max.}$ 238·5 mμ (ε 16,030), $\nu_{max.}$ 1742 and 1230 (21-OAc), 1730 (20-C=O), 1662, 1618, and 866 cm.$^{-1}$ (Δ^4-3-C=O) (Found: C, 71·9; H, 8·2. Calc. for $C_{24}H_{32}O_5$: C, 72·0; H, 8·1%). Taub *et al.*[20] give m. p. 210—215°, $[\alpha]_D$ +145°, $\lambda_{max.}$ 238 mμ (ε 17,000 in MeOH), and describe the isolation of a D-homo-isomer, m. p. 154—157°, $[\alpha]_D$ +95°, of the Δ^4-3-ketone (XX). In the infrared spectrum of our specimen reduced intensity of the band at 1410 cm.$^{-1}$ indicated the presence of some (*ca.* 15%) D-homo-compound.

21-Acetoxy-17-hydroxy-16β-methylpregna-1,4,9-triene-3,20-dione (XVII; R = Me).—(a) *From the 2α,4α-dibromide* (XV; R = Me). To a stirred suspension of calcium carbonate (0·96 g.) and lithium bromide (1·1 g.) in dimethylacetamide (30 ml.) at 96·5° under nitrogen was added a mixture of the 2α,4α-dibromide (2·4 g.) and calcium carbonate (2·4 g.). After 22 hr. the product was isolated as a pale brown solid (1·65 g.; $\lambda_{max.}$ 238 mμ, $E^{1\%}_{1\,cm.}$ 371) by pouring the cooled reaction mixture into 2N-hydrochloric acid (500 ml.). This material (1·6 g.) and Girard's P reagent (0·4 g.) were refluxed for 1 hr., under nitrogen, in methanol (26 ml.) containing acetic acid (1·3 ml.). The fraction not forming a water-soluble derivative was isolated with ethyl acetate and treated with charcoal; concentration of the solution to 15 ml. yielded birefringent prisms (0·89 g., 52%) of the triene (XVII; R = Me), m. p. 219—223°, $[\alpha]_D$ +70°, $[\alpha]_D$ +73° (in dioxan), R.D. in dioxan (*c* 0·067) [α] (*320* mμ) +1810°, $\lambda_{max.}$ 238·5 mμ (ε 15,750), $\nu_{max.}$ 1742 and 1236 (21-OAc), 1728 (20-C=O), 1660 and 888 cm.$^{-1}$ ($\Delta^{1,4}$-3-C=O) (Found: C, 72·1; H, 7·6. Calc. for $C_{24}H_{30}O_5$: C, 72·3; H, 7·6%). Two further crops (0·16 g. and 40 mg.) brought the total yield to 64%. Taub *et al.*[20] give m. p. 208—212°, $[\alpha]_D$ +75°, $\lambda_{max.}$ 238 mμ (ε 15,200) in MeOH. The physical constants for this material recorded[20] by Oliveto *et al.* differ considerably from those given above. A personal communication from the Schering Corporation has confirmed that the constants obtained during the present work are correct.

Hydrolysis of the 21-acetate (XVII; R = Me) (1·5 g.) under nitrogen with potassium hydrogen carbonate in aqueous methanol[7] for 4 hr. at room temperature, and crystallisation of the product from ethyl acetate, gave *17,21-dihydroxy-16β-methylpregna-1,4,9-triene-3,20-dione* (0·65 g.), m. p. 219—225° (cap.), $[\alpha]_D$ +43° (*c* 0·44 in dioxan), $\lambda_{max.}$ 237 mμ (ε 15,800), $\nu_{max.}$ (in Nujol) 1720 (20-C=O), 1660 and 880 cm.$^{-1}$ ($\Delta^{1,4}$-3-C=O) (Found: C, 73·9; H, 8·0. $C_{22}H_{28}O_4$ requires C, 74·1; H, 7·9%).

(b) *From the 2α,4β-dibromide* (XVI; R = Me). Dehydrobromination of the 2α,4β-dibromide as in (a) gave the triene (62%), m. p. 225—228°, $[\alpha]_D$ +71° (*c* 0·4 in dioxan), $\lambda_{max.}$ 238

mμ (ε 15,800). A second crop (10%), m. p. 213—219°, was obtained from the mother-liquors.

(c) *From* 21-*acetoxy*-17-*hydroxy*-16β-*methyl*-5α-*pregn*-9-*ene*-3,20-*dione* (VII; R = Me) *without isolation of the dibromide.* The crude dibromide, prepared from the 16β-methyl-Δ^9-steroid (VII; R = Me) (50 g.) as described above, was obtained as a solution in ethyl acetate. Concentration *in vacuo* at room temperature (nitrogen bubbler) gave a gel, which was dissolved in dimethylacetamide (75 ml.); residual ethyl acetate was removed by evaporation *in vacuo*. This solution was added during 10 min. to a stirred suspension of calcium carbonate (98 g.) and lithium bromide (32 g.) in dimethylacetamide (800 ml.) at 98° under nitrogen. After 40 hr. the mixture was concentrated *in vacuo* to *ca.* 500 ml., cooled, and poured with stirring into 2N-hydrochloric acid (5 l.). The resulting buff solid was washed with sodium hydrogen carbonate solution and then with water until the washings were neutral The crude dry product (43·6 g., 88%), after being purified by treatment with Girard's reagent P and with charcoal, yielded the triene (XVII; R = Me) (19·2 g., 39%), m. p. 221—225°, 214—218° (cap.), $[\alpha]_D$ +71° (*c* 1·45 in dioxan), $\lambda_{max.}$ 238 mμ (ε 15,300). Two further crops brought the total yield to 50%.

An increase in the concentration of the dibromide in the dehydrobromination mixture, other factors being the same, led to increased contamination of the product with the isomeric $\Delta^{4,6,9}$-triene (XXII). This effect was only partially redressed by increasing the proportion of calcium carbonate.

Dehydrobromination at temperatures in the range 90° to 150° provided comparable yields of the triene (XVII; R = Me), the optimum time of reaction decreasing with increasing temperature (*e.g.*, 4 hr. and 130°). Reactions in boiling dimethylacetamide with calcium carbonate were less successful; in one case dehydrobromination of a crude dibromide (1·5 g.; prepared by bromination in acetic acid) led to the isolation of a D-*homo-compound* (*e.g.*, XXIV), (0·27 g.), m. p. 242—245° (cap.), $[\alpha]_D$ −7° (*c* 0·5 in dioxan), R_F 0·78 (Z), $\lambda_{max.}$ 237 mμ (ε 16,000), $\nu_{max.}$ 1734 and 1240 (21-OAc), 1702 (20-C=O), 1662 and 888 cm.$^{-1}$ ($\Delta^{1,4}$-3-C=O) (Found: C, 72·9; H, 7·6. $C_{24}H_{30}O_5$ requires C, 72·3; H, 7·6%). The factors leading to dehydrobromination products containing relatively high proportions of D-homo-isomers remain obscure.

21-*Acetoxy*-17-*hydroxy*-16β-*methylpregna*-4,6,9-*triene*-3,20-*dione* (XXII; R = Me).—The crystalline 2α,4α-dibromide (XV; R = Me) (5·0 g.) was dehydrobrominated with lithium carbonate (4·0 g.) and lithium bromide (2·3 g.) in dimethylacetamide (31 ml.) at 98° for 15 hr. under nitrogen. The crude product (3·3 g.), isolated in the usual manner, had $\lambda_{max.}$ 239 mμ ($E^{1\%}_{1\,cm.}$ 296) and 275 mμ ($E^{1\%}_{1\,cm.}$ 263). This product (3·27 g.) and Girard's reagent P (1·65 g.) were heated at reflux for 45 min. in methanol (50 ml.) containing acetic acid (2·5 ml.). The mixture was poured into 4% sodium hydrogen carbonate solution (500 ml.) and extracted with ethyl acetate, to give the crude 1,4,9-triene (XVII; R = Me) (2·1 g.), $\lambda_{max.}$ 237·5 mμ (ε 14,000). The Girard-forming material (0·6 g.) was isolated with ethyl acetate from the acidified (pH ~1) layer. Purification of this product on Florisil (20 g.) gave the 4,6,9-*triene* (0·26 g.), as birefringent plates (from ethyl acetate), m. p. 227—228° (crystal change to needles at >204°), $[\alpha]_D$ −15° (in dioxan), $\lambda_{max.}$ 282 mμ (ε 26,650), $\nu_{max.}$ 1742 and 1232 (21-OAc), 1725 (20-C=O), 1657 and 875 cm.$^{-1}$ ($\Delta^{4,6}$-3-C=O) (Found: C, 72·2; H, 7·6. $C_{24}H_{30}O_5$ requires C, 72·3; H, 7·6%).

We have not investigated the effect of varying the rate of stirring or the particle size of the lithium carbonate on the ratio of isomeric trienes (XVII and XXII; R = Me) formed.

21-*Acetoxy*-2α-*bromo*-17-*hydroxy*-16β-*methylpregn*-4,9-*diene*-3,20-*dione* (XXI).—The 2α,4β-dibromide (XVI; R = Me) (0·25 g.) in collidine (2·5 ml.) was heated under nitrogen on the steam-bath for 3 hr. The product was isolated with ethyl acetate, triturated with ether, and crystallised from aqueous acetone to give a specimen of the 2-bromo-Δ^4-3-ketone (XXI; R = Me), as plates, m. p. 181—182° (cap.), $\lambda_{max.}$ 242 mμ (ε 12,900).

A similar product, obtained by treating the 2α,4α-dibromide (XV; R = Me) with calcium carbonate and lithium bromide in dimethylacetamide at room temperature (~20°) for 25 days, crystallised from methanol to give the 2α-*bromo*-Δ^4-3-*ketone* (XXI; R = Me), m. p. 171—172° (cap., decomp.), $[\alpha]_D$ +126° (in dioxan), $\lambda_{max.}$ 242 mμ (ε 14,800), $\nu_{max.}$ 1742 and 1236 (21-OAc), 1728 (20-C=O), and 1680 cm.$^{-1}$ (2α-bromo-Δ^4-3-ketone) (Found: C, 59·5; H, 6·6; Br, 16·0. $C_{24}H_{31}BrO_5$ requires C, 60·1; H, 6·6; Br, 16·7%).

The authors thank Miss F. J. Ridley and Messrs. P. H. Depper, L. A. Nicholls, and A. W. G. Stubbings for assistance with the experimental work.

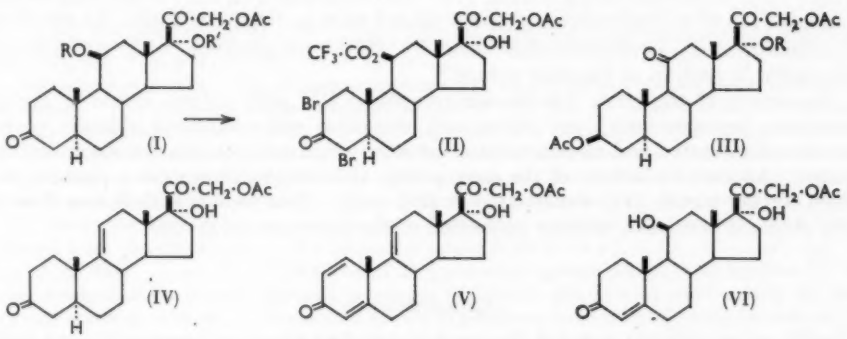
GLAXO LABORATORIES LTD., GREENFORD, MIDDX. [*Received, April* 14*th*, 1961.]

896. *Compounds Related to the Steroid Hormones. Part VII.*[1] *Preparation of* $\Delta^{9(11)}$*-Steroids from* 11β*-Trifluoroacetates.*

By J. Elks and G. H. Phillipps.

Trifluoroacetylation of 21-acetoxy-11β,17-dihydroxy-5α-pregnane-3,20-dione gave the 21-acetate 11,17-bistrifluoroacetate, which could be hydrolysed selectively to the 21-acetate 11-trifluoroacetate. 2,4-Dibromination of this diester proceeded without loss of the trifluoroacetoxy-group, but treatment of the product with calcium carbonate in boiling dimethylacetamide gave 21-acetoxy-17-hydroxypregna-1,4,9-triene-3,20-dione. A similar elimination of the 11β-trifluoroacetoxy-group occurred when the unbrominated 11β-trifluoroacetate was treated with the same reagent.

An earlier publication [2] from these Laboratories described the preparation of some 11β-acyloxy-steroids; for the most part they proved disappointingly prone to undergo elimination under the acid conditions employed in the conversion of a 3-oxo-5α-steroid into its 2,4-dibromo-derivative. In extension of this work, we have examined the bromination and dehydrobromination of 21-acetoxy-17-hydroxy-11β-trifluoroacetoxy-5α-pregnane-3,20-dione (I; $R = CF_3{\cdot}CO$, $R' = H$), in the hope of avoiding some of the difficulties associated with bromination of 3-oxo-steroids containing free 11β-hydroxy-groups and, at the same time, of being able ultimately to hydrolyse the 11β-ester grouping without damaging the cortical side chain.[3]



Treatment of 21-acetoxy-11β,17-dihydroxy-5α-pregnane-3,20-dione (I; $R = R' = H$) with trifluoroacetic anhydride in pyridine and isolation of the product by dilution of the reaction mixture with ether before addition of water gave the 21-acetate 11,17-bistrifluoroacetate (I; $R = R' = CF_3{\cdot}CO$). As the 17-trifluoroacetoxy-group in the bistrifluoroacetate is readily hydrolysed in aqueous solution, dilution of the acylation mixture with water before extraction of the product gave the 21-acetate 11-trifluoroacetate (I; $R = CF_3{\cdot}CO$, $R' = H$) in good yield. Further hydrolysis of this diester with alkali was non-stoicheiometric, 1·3 equiv. of sodium hydroxide in methanol–methylene chloride proving sufficient to remove both the ester groups. However, a better product was obtained by use of two equiv. of alkali, as assessed by reacetylation of the hydrolysis product to the 21-acetate (I; $R = R' = H$) in 74% rather than 57% yield.

Dibromination of the 21-acetate 11-trifluoroacetate (I; $R = CF_3{\cdot}CO$, $R' = H$) in acetic acid gave a crude 2,4-dibromo-compound (II),[3a] which, judged by its infrared

[1] Part VI, preceding paper.
[2] Evans, Green, Hunt, Long, Mooney, and Phillipps, *J.*, 1958, 1529.
[3] (*a*) B.P. 824,109; (*b*) U.S.P. 2,800,489.

absorption,[4] was essentially the 2α,4α-dibromo-isomer. Dehydrobromination of either the crude or the partially purified dibromo-compound (II) by boiling it in dimethylacetamide in the presence of calcium carbonate [5] gave similar products, in which the trifluoroacetoxy-group was no longer present. Purification of the product from the crude dibromo-compound yielded 36·5% of 21-acetoxy-17-hydroxypregna-1,4,9-triene-3,20-dione (V), identical with a sample obtained by dehydration of 21-acetoxy-11β,17-dihydroxypregna-1,4-diene-3,20-dione.[1] The trienedione (V) is a useful source of biologically active 9α-halogeno-compounds.

A somewhat similar reaction involving simultaneous dehydrobromination and elimination of an 11α-methanesulphonyloxy-group has been reported [6] to give a good yield in the preparation of 21-acetoxy-17-hydroxy-16α-methylpregna-1,4,9-triene-3,20-dione.

Elimination of the 11β-trifluoroacetoxy-group by boiling dimethylacetamide containing calcium carbonate also occurred with the unbrominated diester (I; R = CF_3·CO, R′ = H), the Δ^9-steroid (IV) being obtained in high yield. Under similar conditions, the 17-trifluoroacetoxy-group in 3β,21-diacetoxy-17-trifluoroacetoxy-5α-pregnane-11,20-dione (III; R = CF_3·CO) [prepared from the 17-hydroxy-compound (III; R = H) with trifluoroacetic anhydride in pyridine] was not eliminated, but it was apparently hydrolysed during working up with water, the product being simply the 17-hydroxy-compound (III; R = H).

The use of collidine for the dehydrobromination was also examined. The 11-trifluoroacetate (I; R = CF_3·CO, R′ = H) could be recovered after being boiled with collidine, but if the dibromo-compound (II) was treated similarly the sole isolated product, obtained in only 7·5% yield, was the 1,4,9-triene (V). This contrasts with the Patent claim to have obtained 11β,17,21-trihydroxypregna-1,4-diene-3,20-dione from 2,4-dibromo-11β,17,21-tristrifluoroacetoxy-5α-pregnane-3,20-dione by dehydrobromination with collidine and subsequent hydrolysis of the ester groups.[3a]

Treatment of the crude 2,4-dibromo-compound (II) with sodium iodide in acetone containing bromoacetone [7] and subsequent reduction with chromous chloride gave a mixture of saturated and αβ-unsaturated ketones, which still contained trifluoroacetoxy-groups. Alkaline hydrolysis of the ester groups and reacetylation gave a product from which cortisol acetate (VI) was isolated in 13% yield. This yield is little better than the 10% obtained previously without protection of the 11β-hydroxyl group.[2]

Experimental

M. p.s were measured with a Kofler block; optical rotations and ultraviolet and infrared absorptions are for solutions in $CHCl_3$, EtOH, and $CHBr_3$, respectively, unless otherwise stated.

21-Acetoxy-11β,17-bistrifluoroacetoxy-5α-pregnane-3,20-dione (I; R = R′ = CF_3·CO).—21-Acetoxy-11β,17-dihydroxy-5α-pregnane-3,20-dione (1·0 g.) was added to a mixture of pyridine (11 ml.) and trifluoroacetic anhydride (2 ml.) at room temperature, and after 30 min. the mixture was diluted with ether and washed with 2N-hydrochloric acid, aqueous sodium hydrogen carbonate, and water. Removal of the solvent from the dried ethereal solution left a froth (0·6 g.), which showed no absorption for hydroxyl in its infrared spectrum. Addition of water to a cold solution of the froth in methanol gave the *bistrifluoroacetate* as a methanol solvate, m. p. 85—90°, $[\alpha]_D$ +20°, $\nu_{max.}$ 1778 (CF_3·CO_2), 1750 and 1224 (21-OAc), 1734 (20-C=O), 1706 (C=O), and 3620 and 1012 cm.$^{-1}$ (MeOH). The analytical sample was desolvated at 90°/0·1 mm. (Found: C, 54·6; H, 5·7; F, 17·8. $C_{27}H_{32}F_6O_8$ requires C, 54·2; H, 5·4; F, 19·0%).

A solution of the bistrifluoroacetate (50 mg.) in alcohol (4 ml.) and water (1 ml.) became acidic on being heated on a steam-bath for 20 min., and dilution with water then gave the

[4] Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828.
[5] Green and Long, *J.*, 1961, 2532.
[6] Wieland, Heusler, and Wettstein, *Helv. Chim. Acta*, 1960, **43**, 523.
[7] Evans, Hamlet, Hunt, Jones, Long, Oughton, Stephenson, Walker, and Wilson, *J.*, 1956, 4356.

11-monotrifluoroacetate (30 mg.), m. p. 165—170°, with an infrared spectrum identical with that of the material prepared as in the following experiment.

21-Acetoxy-17-hydroxy-11β-trifluoroacetoxy-5α-pregnane-3,20-dione (I; R = CF_3·CO, R′ = H).—21-Acetoxy-11β,17-dihydroxy-5α-pregnane-3,20-dione (4·0 g.) was treated as in the foregoing experiment, but the reaction mixture was poured into water before extraction of the product into ether. The extracted product crystallised from aqueous alcohol, to give the *11-trifluoroacetate* (3·87 g., 78%), m. p. 177—179°, $[\alpha]_D$ +83°, which on further crystallisation from ethyl acetate–hexane gave the analytical sample, m. p. 181—182°, $[\alpha]_D$ +84° (Found: C, 59·6; H, 6·5; F, 10·3. $C_{25}H_{33}F_3O_7$ requires C, 59·7; H, 6·6; F, 11·3%), $\nu_{max.}$ 1774 (CF_3·CO_2), 1744 and 1222 (21-OAc), 1722 (20-C=O), and 1708 cm.$^{-1}$ (C=O).

Hydrolysis of 21-Acetoxy-17-hydroxy-11β-trifluoroacetoxy-5α-pregnane-3,20-dione.—The diester (2·0 g.) in methylene chloride (80 ml.) was treated under nitrogen with 0·104N-sodium hydroxide in methanol (84 ml., 2 equiv.), and after 20 min. the solution was acidified with 1% acetic acid (25 ml.), concentrated to small bulk *in vacuo*, and diluted with water. The solid precipitate (1·37 g., 95%), m. p. 215—225°, showed no bands for acetate or trifluoroacetate in its infrared spectrum, and on acetylation with acetic anhydride and crystallisation gave the 21-acetate (I; R = R′ = H) (74%), m. p. 220—223°, $[\alpha]_D$ +79·5°.

In another experiment with 1·3 equiv. of alkali both the ester groups were removed but after reacetylation the 21-acetate (I; R = R′ = H) was obtained in only 57% yield.

21-Acetoxy-2,4-dibromo-17-hydroxy-11β-trifluoroacetoxy-5α-pregnane-3,20-dione (II).—Bromine (0·42 ml.) was added during 1 min. to a stirred solution of the 11-trifluoroacetate (I; R = CF_3·CO, R′ = H) (6·0 g.) in acetic acid (90 ml.) at room temperature, and after 30 min. the solution was poured into water to precipitate the crude dibromo-compound (7·83 g., 99%), m. p. 120—135°, $[\alpha]_D$ +57°. Crystallisation from ether–hexane, then benzene–hexane, gave dense prisms of the *2,4-dibromo-compound*, m. p. 165° (decomp.), $[\alpha]_D$ +65° (Found: C, 46·2; H, 5·1; Br, 23·5; F, 8·3. $C_{25}H_{31}Br_2F_3O_7$ requires C, 45·5; H, 4·7; Br, 24·2; F, 8·6%), $\nu_{max.}$ 1778 (CF_3·CO_2), 1748 (21-OAc and 2,4-dibromo-3-ketone), 1225 (21-OAc), and 1726 cm.$^{-1}$ (20-C=O) (lit.,[3a] m. p. 175—182°).

Dehydrobromination of the Dibromo-compound (II).—(a) *With calcium carbonate in dimethylacetamide.* The foregoing crude dibromo-compound (II) (2·5 g.) in cold dimethylacetamide (5 ml.) was added during 1·5 min. to a refluxing suspension of finely divided calcium carbonate (2·0 g.) in dimethylacetamide (20 ml.). After 12 min. the suspension was concentrated *in vacuo*, cooled, and poured into water (200 ml.). The aqueous suspension was acidified with 2N-hydrochloric acid, the product was extracted with methylene chloride, and the extract was washed with 2N-hydrochloric acid, aqueous sodium hydrogen carbonate, and water. Removal of solvent from the dried extract *in vacuo* left a brown solid (1·35 g.), m. p. 195—210°, $\lambda_{max.}$ 239 mμ ($E^{1\%}_{1\,cm.}$ 354). A solution of the solid (1·25 g.) in ethyl acetate (25 ml.) and benzene (75 ml.) was decolorised by passage through a column of Florisil (50 g.) and elution with the same solvent mixture (600 ml.). The eluted steroid crystallised from ethyl acetate–hexane to give 21-acetoxy-17-hydroxypregna-1,4,9-triene-3,20-dione (V) (0·524 g., 36·5%), m. p. 225—228°, $[\alpha]_D$ +51°, $\lambda_{max.}$ 239 mμ (ε 14,000), with an infrared spectrum identical with that of material prepared by dehydration of 21-acetoxy-11β,17-dihydroxypregna-1,4-diene-3,20-dione.[1]

A similar experiment starting with crystallised dibromo-compound (II) (500 mg.) gave a crude product (260 mg.), m. p. 190—205°, $\lambda_{max.}$ 239 mμ ($E^{1\%}_{1\,cm.}$ 370), with an infrared spectrum similar to that of the above crude product.

(b) *With collidine.* The crude dibromo-compound (II) (3·85 g.) was added to boiling collidine (30 ml.) containing water (0·1 ml.) and after 1 hr. the solvent was removed at 100° *in vacuo*. A solution of the residue in methylene chloride was washed with 2N-hydrochloric acid, aqueous sodium hydrogen carbonate, and water. Removal of solvent from the dried solution left a gum (1·8 g.), $\lambda_{max.}$ 240 mμ ($E^{1\%}_{1\,cm.}$ 334) (Found: Br, 11·2%), which from its infrared spectrum contained <50% of $\Delta^{1,4}$-3-oxo-compounds.

The crude product (1·7 g.) and Girard reagent P (1·0 g.) were boiled under reflux for 30 min. in ethanol (30 ml.) and acetic acid (3 ml.), and the cooled solution was poured into an excess of aqueous sodium hydrogen carbonate. The unreactive $\Delta^{1,4}$-3-ketones (0·8 g.) were extracted into ethyl acetate and after treatment with Florisil as in (a) crystallised to give the $\Delta^{1,4,9}$-triene (V) (180 mg., 7·5%), m. p. 217—221°, $[\alpha]_D$ +50°.

21-Acetoxy-17-hydroxy-5α-pregn-9-ene-3,20-dione (IV).—21-Acetoxy-17-hydroxy-11β-trifluoroacetoxy-5α-pregnane-3,20-dione (0·5 g.) was added to a boiling suspension of finely

divided calcium carbonate (0·35 g.) in dimethylacetamide (5 ml.) and after 13 min. the cooled suspension was poured into water and acidified with 2N-hydrochloric acid. The precipitated product (0·37 g.), m. p. 230—240°, crystallised from ethyl acetate to give the Δ^9-compound (IV) as plates (0·18 g., 47%), m. p. 247—253°, with an infrared spectrum identical with that of a sample prepared from the 11β-alcohol (I; R = R′ = H).[2]

When the 11-trifluoroacetate (2·0 g.) was treated with collidine as in the foregoing experiment (b), starting material (1·65 g.), m. p. 177—181°, was recovered.

3β,21-Diacetoxy-17-trifluoroacetoxy-5α-pregnane-11,20-dione (III; R = CF_3·CO).—3β,21-Diacetoxy-17-hydroxy-5α-pregnane-11,20-dione (III; R = H) (1·0 g.) in pyridine (11 ml.) was treated with trifluoroacetic anhydride (2 ml.) and after 10 min. the mixture was diluted with ether. The solvent was removed from the washed and dried solution to leave crystals (1·1 g.), m. p. 163—168°, which, on recrystallisation from ethyl acetate–hexane, gave the *17-trifluoroacetate* (670 mg.), m. p. 166—168°, $[\alpha]_D$ +2° (Found: C, 59·8; H, 6·4. $C_{27}H_{35}F_3O_8$ requires C, 59·55; H, 6·5%), $\nu_{max.}$ 1784 (CF_3·CO_2), 1748 and 1230 (21-OAc), 1725 (20-C=O), and 1712 cm.$^{-1}$ (11-C=O).

When the 17-trifluoroacetate was treated with boiling dimethylacetamide containing calcium carbonate for 10 min., the product, isolated as in above experiments, showed only low general absorption in the ultraviolet region and was identified from its infrared spectrum as the 17-hydroxy-compound (III; R = H).

Cortisol 21-Acetate (VI).—The crude 21-acetoxy-2,4-dibromo-17-hydroxy-11β-trifluoroacetoxy-5α-pregnane-3,20-dione (II) (3·85 g.) was treated with sodium iodide (19 g.) in acetone (90 ml.) containing bromoacetone, as described previously.[7] Part (2·5 g.) of the crude product (2·6 g.), $\lambda_{max.}$ 237·5 mμ ($E^{1\%}_{1\,cm.}$ 199), was hydrolysed with 0·1N-sodium hydroxide in methanol (100 ml.) under nitrogen for 15 min. The solution was neutralised with acetic acid, concentrated, and diluted with water. The precipitate was reacetylated with acetic anhydride in pyridine, giving a mixture of saturated and unsaturated ketones (1·5 g.), $\lambda_{max.}$ 242 mμ ($E^{1\%}_{1\,cm.}$ 194). Segration of the αβ-unsaturated ketone in the product by means of its Girard derivative and crystallisation from ethyl acetate gave cortisol 21-acetate (297 mg., 13%), m. p. 216—220°, $\lambda_{max.}$ 240 mμ (ε 15,000), with an infrared spectrum (in Nujol) resembling that of an authentic sample.

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX. [*Received, April 14th*, 1961.]

---

897. *The Mechanism of Hydramine Fission.*

By A. CHATTERJEE, S. K. SRIMANY, and (MISS) B. CHAUDHURY.

Hydramine fission of β-hydroxyphenethylamine and some of its substitution products in presence of hydrochloric acid has been studied. The degradation products are either aromatic ketones or aldehydes. Aldehydes are formed when the phenyl nucleus is substituted in the *ortho-* or *para*-position by electron-releasing groups, whereas their *meta*-orientation or *para-* and *ortho*-substitution by electron-attracting groups favours formation of ketones, the latter being also produced from unsubstituted amine. A possible mechanism of the reaction is discussed.

β-HYDROXYPHENETHYLAMINES,[1] on treatment with mineral or organic acid at elevated temperatures, split off nitrogen as amine or ammonia and are transformed into aromatic ketones. In recent years Auterhoff and Roth [2] and Fellman [3] studied the hydramine fission and showed the β-hydroxyphenethylamines, when heated with phosphoric acid, produce phenylacetaldehydes if the α-carbon is unsubstituted but that in other cases phenylacetones are the major products. Fellman [3] also predicted that similar compounds would arise from the action of 20% aqueous hydrochloric acid. The mechanism of the

[1] Reti, in " The Alkaloids," ed. Manske, Academic Press, New York, 1953, Vol. III, p. 339; Rabe and Schneider, *Annalen*, 1909, **365**, 377.
[2] Auterhoff and Roth, *Arch. Pharm.*, 1956, **289**, 470.
[3] Fellman, *Nature*, 1958, **182**, 311.

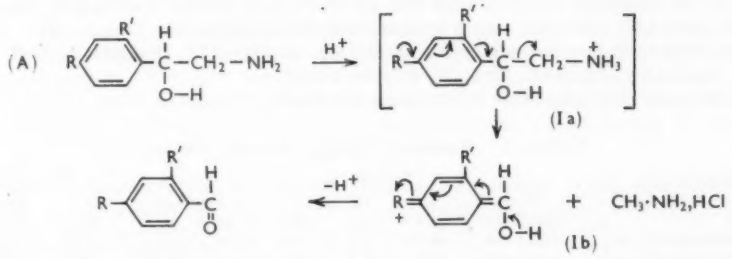
reaction has been explained by Auterhoff and Roth [2] as involving pinacol–pinacolone rearrangement.

The present authors have studied the hydramine fission of various β-hydroxyphenethylamines in 10—20% hydrochloric acid. It has been observed that the nature and orientation of substituents in the phenyl nucleus play important roles in determining the course of fission. The results are set out in Table 1.

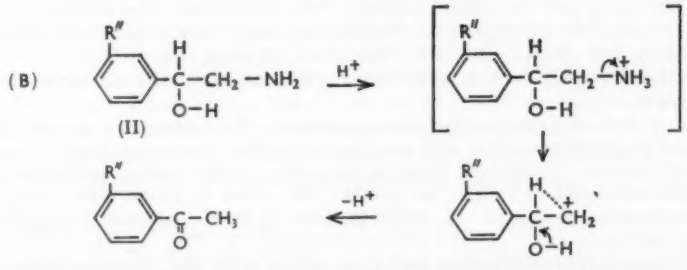
TABLE 1. *Products of fission in* HCl.

No.	β-Hydroxyphenethylamine	Product
1	4-Methoxy	*p*-Methoxybenzaldehyde
2	2-Methoxy	*o*-Methoxybenzaldehyde
3	3-Methoxy	*m*-Hydroxyacetophenone
4	4-Nitro	*p*-Nitroacetophenone
5	4-Hydroxy	*p*-Hydroxybenzaldehyde
6	3-Hydroxy	*m*-Hydroxyacetophenone
7	Unsubst.	1,3-Diphenylcyclobutadiene (*via* acetophenone)
8	4-Methyl	*p*-Methylbenzaldehyde
9	3-Methyl	*m*-Methylacetophenone

para- and *ortho*-Methoxyl, -hydroxyl, or -methyl groups greatly facilitate the hydramine fission; with *meta*-substituted or the unsubstituted amine this degradation is extremely sluggish and requires concentrated acid (which also demethylates a methoxyl group; no. 3). It seems that the mechanism is different from that proposed earlier: [2,3] when electron relay is possible, mechanism (A) operates; when this relay is not possible, transfer



of electrons from the β- to the α-carbon atom cannot take place and nitrogen is eliminated as ammonia (mechanism B). In case of β-hydroxy-4-nitrophenethylamines, the hydramine fission follows path (B), resulting in the ketone; but the yield is extremely poor because of the electron-deficiency at carbon *para* to the nitro-group.



It seems that hydramine fission in presence of hydrochloric acid involves a unimolecular reaction and the formation of an 'onium ion; its kinetics are being studied. The reaction with β-hydroxyphenethylamine gave, unexpectedly, 1,3-diphenylcyclobutadiene; the predecessor of this was acetophenone which was isolated as its 2,4-dinitrophenylhydrazone when dinitrophenylhydrazine was added to reaction mixture.

Experimental

M. p.s were determined on a Kofler block. β-Hydroxyphenethylamines were prepared by the methods of Chaudhury and Chatterjee [4] and Corrigan *et al.*[5] with some modifications: those which did not crystallise were isolated as crystalline *N*-cinnamoyl derivatives or hydrochlorides. For hydramine fission these derivatives were employed. The yields of the carbonyl compounds were determined from those of their 2,4-dinitrophenylhydrazones (prepared *in situ*); they were 75—80% except that β-hydroxy-4-nitrophenethylamine gave only a 30% yield. Only one carbonyl derivative was isolated in each case.

Analyses were by Mr. W. Manser, Zürich, Switzerland, or Mr. B. Bhattacharya, University College of Science and Technology, Calcutta.

New *compounds* are listed in Table 2.

Table 2. *β-Hydroxyphenethylamines.*

Compound no. (cf. Table 1)	M. p.	Found (%) C	H	N	OMe	Formula	Required (%) C	H	N	OMe
2 (Base)	120—121°	64·6	7·6	8·5	19·0	$C_9H_{13}O_2N$	64·7	7·8	8·4	18·5
8 (Base)	68—69	71·5	8·55	9·3	—	$C_9H_{13}ON$	71·5	8·6	9·3	—
9 (Cinnamoyl deriv.)	139—140	76·6	6·5	4·9	—	$C_{18}H_{19}O_2N$	76·8	6·8	4·9	—

β-*Hydroxy*-3-*methoxyphenethylamine.*—ω-Bromo-3-methoxyacetophenone [6] (13 g.) was converted into its hexamethylenetetramine derivative in dry monochlorobenzene (29 ml.) at 50—52°. This was decomposed with alcoholic hydrochloric acid into the ω-amino-ketone, isolated as its crystalline hydrochloride (5·3 g.) which with sodium borohydride (6 g.) in dry methanol (200 ml.) afforded oily β-hydroxy-3-methoxyethylamine (2 g.). The *cinnamate* (3 g.) crystallised from ethyl acetate in needles, m. p. 131—132° (Found: C, 72·3; H, 6·5; N, 4·6. $C_{18}H_{19}O_3N$ requires C, 72·2; H, 6·7; N, 4·7%).

The *compounds* listed in Table 3 were prepared analogously.

Table 3. *Further β-hydroxyphenethylamines.*

Compound no. (see Table 1)	M. p.	Found (%) C	H	N	Formula	Required (%) C	H	N
4 (Base)	136—137°	52·8	5·4	15·2	$C_8H_{10}O_3N_2$	52·7	5·5	15·3
5 (Hydrochloride)	167—169	50·7	6·4	7·5	$C_8H_{11}O_3N,HCl$	50·6	6·3	7·4
6 (Hydrochloride)	157—158	50·7	6·4	7·5	$C_8H_{11}O_3N,HCl$	50·6	6·3	7·4
7 (Cinnamoyl deriv.).....	176—178	76·45	6·4	5·3	$C_{17}H_{17}O_2N$	76·4	6·3	5·2

Hydramine Fissions.—*N*-(β-Hydroxy-3-methoxyethyl)cinnamamide (0·5 g.) was heated at 120° for 4 hr. in a sealed tube with 50% alcoholic hydrochloric acid (5 ml.). The mixture was then diluted with a little water and extracted with ether (3 × 15 ml.). The ethereal layer was freed from acid and was dried (Na_2SO_4). The residue left after removal of the solvent furnished anisaldehyde 2,4-dinitrophenylhydrazone which crystallised from ethyl acetate in red flakes, m. p. 250° (Found: N, 17·9. Calc. for $C_{14}H_{12}N_4O_5$: N, 17·7%).

Fission of compounds 2—6, 8, and 9 was carried out similarly with minor variations (see Tables 1 and 4).

Fission of N-(β-*Hydroxyphenylethyl*)*cinnamamide.*—The amide (0·5 g.) was heated with concentrated hydrochloric acid (7 ml.) and 2,4-dinitrophenylhydrazine (0·4 g.) in a sealed tube at 130—135° for 4 hr. Cooling and filtration then gave a reddish-orange residue that crystallised from glacial acetic acid in needles, m. p. 236—237° alone or mixed with acetophenone 2,4-dinitrophenylhydrazone (Found: C, 56·2; H, 4·2; N, 18·7. Calc. for $C_{14}H_{12}O_4N_4$: C, 56·0; H, 4·0; N, 18·7%).

When β-hydroxyphenethylamine had been heated with 20% aqueous hydrochloric acid alone at 120—130° for 15 hr., working up as described above gave 1,3-diphenylbutadiene that crystallised in good yield from alcohol in plates, m. p. and mixed m. p. 97—98° (Found: C, 94·2;

[4] Chaudhury and Chatterjee, *J. Indian Chem. Soc.*, 1959, **36**, 585.
[5] Corrigan, Langerman, and Moore, *J. Amer. Chem. Soc.*, 1945, **67**, 1894.
[6] *Org. Synth.*, 1947, Coll. Vol. II, p. 480.

TABLE 4. *Fission products* (cf. Table 1).

Amine no. (cf. Table 1)	HCl (%)	Temp.	Time (hr.)	2,4-Dinitrophenylhydrazone of product M. p.	N (Found, %)	Formula	N (Calc., %)
1 (Cinnamoyl deriv.) ...	10	120°	4	250°	17·9	$C_{14}H_{12}O_5N_4$	17·7
2 (Base)	20	120	15 or 10	237—239	17·7	,,	17·7
3 (Cinnamoyl deriv.) ...	20	130—140	65	239—240	17·9	,,	17·7
4 (Base)	20	120	60	255	20·45	$C_{14}H_{11}O_6N_5$	20·3
5 (Hydrochloride)	10	120	15	280	18·6	$C_{13}H_{10}O_5N_4$	18·5
6 (Hydrochloride)	20	130	65	240	17·8	$C_{14}H_{12}O_5N_4$	17·7
7 (Cinnamoyl deriv.) ...	20	120	4	236—237	18·7	$C_{14}H_{12}O_4N_4$	18·7
8 (Hydrochloride)	10	120	15	233	18·8	,,	18·7
9 (Hydrochloride)	20	130	65	207	17·9	$C_{15}H_{14}O_4N_4$	17·8

H, 5·85%; *M*, 202. Calc. for $C_{16}H_{12}$: C, 94·1; H, 5·9%; *M*, 204), $\lambda_{max.}$ 249 (log ε 3·15) and 287·5 mμ (log ε 4·22) in EtOH.

DEPARTMENT OF ORGANIC CHEMISTRY, THE UNIVERSITY COLLEGE OF SCIENCE, CALCUTTA, INDIA. [*Received, February 27th*, 1961.]

898. *The Chemistry of Fungi. Part XXXIX.*[1] *The Structure of Monascin.*

By B. C. FIELDING, J. S. E. HOLKER, D. F. JONES, A. D. G. POWELL, K. W. RICHMOND, ALEXANDER ROBERTSON, and W. B. WHALLEY.

Structure (III), suggested for monascin, is shown to be compatible with the physical and chemical properties of the parent pigment and its derived compounds. Evidence has been obtained that the parent pigment may contain small amounts of the bis-homologue (V). The nuclear magnetic resonance spectra of monascin and its derivatives are discussed in an Appendix.

IN 1895 it was shown [2] that the fungus *Monascus purpureus* Went. was the organism responsible for the colour of " Red Rice " ("Ang Khak "), a native preparation used as a colouring matter for foodstuffs and alcoholic beverages in parts of Java and China, and which was made by allowing the fungus to grow on the surface of boiled rice.[3] In 1932 Karrer and Saloman [4] described the isolation of a yellow pigment, monascin, from " Red Rice," and at about the same time Nishikawa [5] reported the isolation of a red compound, monascorubrin, together with a yellow compound, monascoflavin (apparently identical with monascin) from a culture of *M. purpureus* grown on a synthetic medium. More recently a systematic survey in this Department of the metabolites of the *Monascus* genus [6] has resulted in the isolation of monascin and rubropunctatin from *M. rubropunctatus* Sâto, monascin and " monascorubrin " from *M. purpureus* Went., and monascin from *M. rubiginosus* Sâto. We have described the structural elucidation of rubropunctatin (I),[1,1a] and have made a preliminary report [7] on the nature of" monascorubrin " in which it was shown by mass-spectrometric examination of suitable derivatives that this substance is a mixture of minor amounts of rubropunctatin (I) with a higher homologue, monascorubrin. Since oxidation of the monascorubrin–rubropunctatin mixture gave octanoic acid

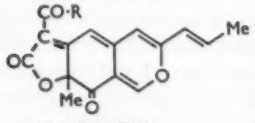
[1] Part XXXVIII, Haws and Holker, *J.*, 1961, 3820.
[1a] Haws, Holker, Kelly, Powell, and Robertson, *J.*, 1959, 3598.
[2] Went, *Ann. d. Sci. Nat. Bot.*, 1895, [8], **1**, 1.
[3] Vorderman, *Analecta ob Cromatologisch Gebied.* II. *Geneesh. Fydschrift voor Ned. Indie*, 1894, **34**, No. 5.
[4] Karrer and Saloman, *Helv. Chim. Acta*, 1932, **15**, 18.
[5] Nishikawa, *J. Agric. Chem. Soc. Japan*, 1932, **8**, 1007.
[6] Powell, Robertson, and Whalley, *Chem. Soc. Special Publ.*, No. 5, 1957, p. 27.
[7] Fielding, Haws, Holker, Powell, Robertson, Stanway, and Whalley, *Tetrahedron Letters*, 1960, No. 5, 24.

and smaller amounts of hexanoic acid, whereas under similar conditions rubropunctatin gave only hexanoic acid, it has been suggested that monascorubrin has structure (II), differing from rubropunctatin (I) only in the length of the saturated side-chain. The present paper is concerned with the third of these metabolites, monascin.

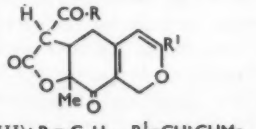
In preliminary examinations of monascin Karrer and his co-workers [4,8] showed that it was an optically active yellow pigment, which seemed to have the molecular formula, $C_{20}H_{24}O_5$. The compound was devoid of methoxyl groups and did not give a ferric reaction. Although it contained one active hydrogen atom (Zerewitinoff), and was precipitated by carbon dioxide from solution in sodium hydroxide, monascin was recovered unchanged after attempted acetylation and benzoylation. Oxidation formed hexanoic, acetic, and oxalic acid, and ozonolysis produced acetaldehyde and methylglyoxal. Hydrogenation of monascin in the presence of a platinum catalyst, and termination of the reaction after absorption of one molecular equivalent of hydrogen, gave small amounts of a compound, m. p. 130—131°, which was formulated as a dihydro-derivative. Exhaustive hydrogenation of monascin in acetic acid with a platinum catalyst resulted in the uptake of four molecular equivalents of hydrogen to give an oily perhydro-derivative. A microcrystalline dihydro-derivative was isolated by reduction of monascin with zinc and acetic acid.

It was apparent that the formula, $C_{20}H_{24}O_5$, suggested for monascin, could not be regarded as rigidly established and, indeed, our analyses on monascin and its derivatives were more compatible with the formula $C_{21}H_{26}O_5$ for the parent pigment. To differentiate between these formulæ tetrahydromonascin (see below) was analysed in the mass spectrometer when, despite extensive fragmentation, the peak due to the largest ion was at *m/e* 362, corresponding to the formula $C_{21}H_{30}O_5$ for tetrahydromonascin, and hence to $C_{21}H_{26}O_5$ for monascin.

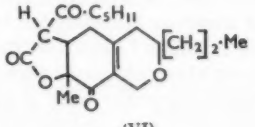
It was tempting to suggest at an early stage that monascin might be a tetrahydro-derivative of rubropunctatin for the following reasons: (*a*) monascin and rubropunctatin (I) are co-metabolites of *M. rubropunctatus*, (*b*) both give hexanoic acid and acetaldehyde, on oxidation and ozonolysis respectively, and (*c*) the molecular formulæ differ only by four hydrogen atoms. The evidence obtained in the present investigation strongly supports this hypothesis and suggests that monascin has structure (III). For convenience the reactions to be discussed will be interpreted in terms of this structure.



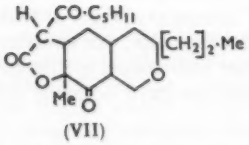
(I); R = C_5H_{11}
(II); R = C_7H_{15}



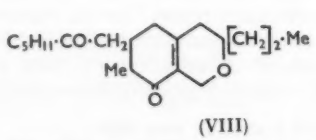
(III); R = C_5H_{11}, R^1 = CH:CHMe
(IV); R = C_5H_{11}, R^1 = $[CH_2]_2$·Me
(V); R = C_7H_{15}, R^1 = CH:CHMe



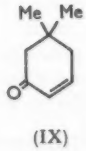
(VI)



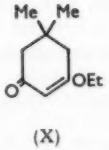
(VII)



(VIII)



(IX)



(X)

Dihydro- (IV), tetrahydro- (VI), and hexahydro- (VII) derivatives of monascin have been prepared by carefully controlled hydrogenation. In this connection the product, m. p. 130—131°, reported as a dihydro-derivative by Karrer and Saloman [4] appears to be the tetrahydro- (VI) (m. p. 135°) rather than the dihydro-derivative (IV) (m. p. 119—121°). Further hydrogenation of hexahydromonascin occurred readily to give an oil. However,

[8] Geiger and Karrer, *Helv. Chim. Acta*, 1941, **24**, 289.

since the ultraviolet absorption spectrum of hexahydromonascin shows no significant end-absorption, it seems likely that, in agreement with structure (VII), this compound contains no olefinic bonds. Hence, the further hydrogenation of hexahydromonascin must involve reduction of carbonyl functions. In agreement with this view, the infrared spectrum of the hexahydro-derivative shows strong absorption in the carbonyl region but no bands which could be attributed either to a hydroxyl group or a double bond, whereas the oily perhydro-substance shows hydroxyl absorption and a significant decrease in the intensity of carbonyl absorption.

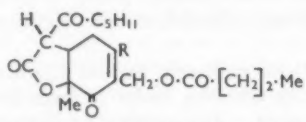
In agreement with structures (III) and (IV) for monascin and its dihydro-derivative, respectively, ozonolysis of (III) gave acetaldehyde whereas, under comparable conditions, (IV) gave no volatile aldehydic or ketonic fragment. The reported [8] isolation of methylglyoxal from ozonolysis of monascin in carbon tetrachloride has been reinvestigated. Thus, in an attempted isolation of methylglyoxal as its 2,4-dinitrophenylosazone, a small amount of a sticky red solid (3% of the calculated amount for the presence of one $\rangle C{:}CH{\cdot}CMe{:}C\langle$ group in the formula $C_{21}H_{26}O_5$) was obtained; it had an infrared spectrum similar to that of authentic methylglyoxal 2,4-dinitrophenylosazone. In view of the very low yield of this product, it seems likely that the compound is an artefact and has no direct structural implication.

The suggested structures for monascin and its hydro-derivatives are compatible with the ultraviolet absorption spectra. Thus, in agreement with the presence of a fully substituted αβ-unsaturated ketone system in structure (VI) for tetrahydromonascin, the spectrum has $\lambda_{max.}$ 244 and 320 mμ (log ε 4·01 and 1·93), and the nuclear magnetic resonance spectrum shows no peak which could be attributed to vinyl hydrogen. Empirical calculation of the expected $\lambda_{max.}$ for the linear conjugated system in structure (IV) for dihydromonascin gives: 215 (parent enone)[9] + 30 (double-bond extending conjugation)[9] + 10 (α-substituent)[9] + 12 (β-substituent)[9] + 18 (γ-substituent)[9] + 39 (homoannular diene component)[9] + 50 (auxochromic ethereal oxygen)[10] = 374 mμ. Since the principal high-intensity absorption band occurs at $\lambda_{max.}$ 365 mμ (log ε 4·18) the agreement with the calculated figure is reasonable, particularly when it is realised that the bathochromic effect of 50 mμ due to the ethereal oxygen atom is assessed by comparison with a limited number of compounds in which the analogy is not particularly close.[10] Finally, the hypsochromic shift of 25 mμ observed on conversion of monascin into its dihydro-derivative is lower than the more usual figure of 30 mμ associated with the removal of a conjugated double bond from a linear conjugated unsaturated ketone. This may be due to the fact that whereas the π-*p*-conjugation of the auxochromic oxygen is fully exerted in the linear conjugated system of dihydromonascin, the same conjugation in monascin is not fully exerted owing to the crossed π–π-conjugation of the propenyl double bond.

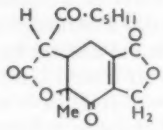
Reduction of tetrahydromonascin with zinc and acetic acid at room temperature gave tetrahydroapomonascin (VIII), a small amount of hexahydromonascin (VII), and carbon dioxide in an amount proportional to the amount of compound (VIII) formed. This reductive expulsion of carbon dioxide from tetrahydromonascin is reminiscent of the behaviour of rubropunctatin derivatives under similar conditions [10a] and is associated with the presence of the structural unit $R{\cdot}CO{\cdot}\overset{|}{C}{\cdot}CO{\cdot}O{\cdot}\overset{|}{C}{\cdot}CO{\cdot}R'$. Unlike monascin and its hydrogenated derivatives, tetrahydroapomonascin is devoid of active hydrogen (Zerewitinoff) and is insoluble in dilute sodium hydroxide. Hence the acidity of compounds (III), (IV), (VI), and (VII) must be associated with the tertiary hydrogen attached to the α-carbon of the β-ketolactone system. Reduction of monascin under similar conditions also gave carbon dioxide, but in this case no other recognisible product could be isolated. In direct contrast, hexahydromonascin was unchanged after treatment with zinc and acetic acid at room temperature and it appears, therefore, that the double bond of the

[9] Fieser and Fieser, "Steroids," Reinhold Publishing Corporation, New York, 1959, pp. 18—21.
[10] Bowden, Braude, and Jones, *J.*, 1946, 948.

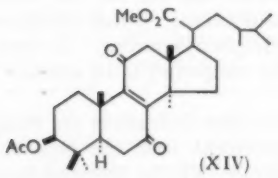
αβ-unsaturated ketone group in monascin and its tetrahydro-derivative is necessary for reduction under these very mild conditions. This is in agreement with similar findings in the steroid series where reduction of α-ketols and their acetates with bivalent metals is greatly facilitated by the presence of double bonds, halogen atoms, or additional acetoxyl groups attached to the carbon atom alpha to the ketol structure.[11]



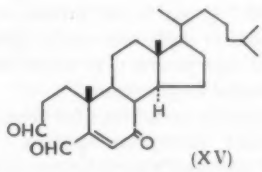
(XI); R = CHO (XII); R = CO_2H



(XIII)

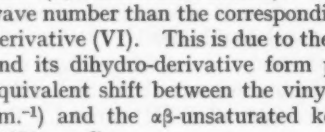


(XIV)

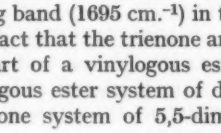


(XV)

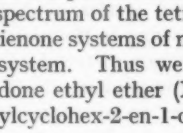
The infrared spectra of monascin and its derivatives support the suggested structures. Thus, the spectrum of tetrahydroapomonascin (VIII) has bands at **1709** (side-chain ketonic carbonyl), **1656**, and **1629sh** cm.$^{-1}$ (αβ-unsaturated ketone). Hexahydromonascin (VII) has bands at **1786** (γ-lactone), **1739** (cyclohexanone carbonyl), **1718** cm.$^{-1}$ (side-chain ketonic carbonyl). The high wave-numbers of the γ-lactone and cyclohexanone bands in this spectrum are in keeping with their relationship in an α-ketol lactone system, since it is known that the ester and ketonic carbonyl bands of α-ketol esters are similarly displaced.[12] Corresponding shifts are also apparent in the spectrum of tetrahydromonascin (VI) which has bands at **1786** (displaced γ-lactone), **1718** (side-chain ketonic carbonyl), **1695** (displaced carbonyl stretch of αβ-unsaturated ketone), and **1623** cm.$^{-1}$ (double-bond stretch of αβ-unsaturated ketone). The carbonyl stretching regions in the spectra of monascin (III) and its dihydro-derivative (IV) are very similar, both having bands at **1785** (displaced γ-lactone), **1715** (side-chain ketonic carbonyl), **1669**, and **1628** cm.$^{-1}$ (αβ-unsaturated ketone). The band at **1669** cm.$^{-1}$ in these compounds is at a lower wave number than the corresponding band (**1695** cm.$^{-1}$) in the spectrum of the tetrahydro-derivative (VI). This is due to the fact that the trienone and dienone systems of monascin and its dihydro-derivative form part of a vinylogous ester system. Thus we find an equivalent shift between the vinylogous ester system of dimedone ethyl ether (X) (**1634** cm.$^{-1}$) and the αβ-unsaturated ketone system of 5,5-dimethylcyclohex-2-en-1-one (IX) (**1670** cm.$^{-1}$).



(XVI)



(XVII)



(XVIII)

Direct chemical evidence has been obtained for the presence of a vinyl ether system in dihydromonascin (IV). Thus, oxidation with sodium dichromate in aqueous acetic

[11] Rosenfeld, *J. Amer. Chem. Soc.*, 1957, **79**, 5540.

[12] Bellamy and Williams, *J.*, 1957, 861; Dickson and Page, *J.*, 1955, 447; Jones and Herling, *J. Org. Chem.*, 1954, **19**, 1252.

acid gave a mixture of the formyl-butyrate ester (XI) and the corresponding carboxylic acid (XII). The former compound was converted into the latter by further oxidation under similar conditions. Hydrolysis of the acid-ester (XII) gave n-butyric acid and the dilactone (XIII). The formyl-ester (XI) similarly gave butyric acid on hydrolysis but in this case the second product was a gum. The dilactone (XIII) has also been prepared directly from both monascin and its dihydro-derivative by oxidation with chromic oxide in sulphuric acid, in conditions where tetrahydromonascin is relatively stable.

The presence of an aldehyde group in compound (XI) and a carboxyl group in (XII) has been demonstrated. Thus, the former compound reduced Tollens's reagent and readily gave a crystalline mono-2,4-dinitrophenylhydrazone whereas, under similar conditions the acid (XII) and the dilactone (XIII) reacted very slowly to give amorphous products. The acid (XII) reacted rapidly with sodium hydrogen carbonate, and with diazomethane gave a neutral amorphous substance which seems to be essentially the methyl ester, since it generated the dilactone (XIII) on hydrolysis. The ultraviolet absorption spectra of the aldehyde (XI) and the acid (XII) had $\lambda_{max.}$ 238, 324 mμ (log ε 3·95, 2·24) and $\lambda_{max.}$ 242 mμ (log ε 3·85), respectively. The *K*-band due to the enedione chromophore in the aldehyde (XI) is at a very low wavelength compared with the band at 270 mμ owing to the similar chromophore in methyl 3-acetoxy-7,11-dioxoeburic-8-en-21-oate (XIV).[13] However, in the latter compound both carbonyl groups of the chromophore are present as keto-groups rigidly locked in a cyclic system, whereas in the former, one of the carbonyl groups is in an aldehyde function. A better analogy to the aldehyde (XI) is provided by compound (XV), which has the *K*-band at 242 mμ [14] in close agreement with the spectrum of (XI).

In accordance with the presence of an αβ-unsaturated lactone ring in the dilactone (XIII), this compound, unlike monascin, gave a positive Legal test under the modified conditions of Paist, Blout, Uhle, and Elderfield.[15] Furthermore, the dilactone reduced Tollens's reagent. This is in agreement with the αβ-unsaturated γ-lactone system in structure (XIII) being unsubstituted at the γ-position, since compounds containing this structural unit are known to isomerise under the alkaline conditions of this test to give the anions of the corresponding γ-formyl-carboxylic acids.[15] The acid (XII) also reduced Tollens's reagent, again owing to the formation of an aldehyde. Zerewitinoff estimation on the dilactone showed two active hydrogen atoms compared with one in dihydromonascin. Since β-cyclohexyl-$\Delta^{\alpha,\beta}$-butenolide and other αβ-unsaturated γ-lactones give values of from half to one active hydrogen atom in this estimation,[15] the value for compound (XIII) is reasonable. The ultraviolet absorption spectrum of this compound provides further evidence for the structural features present. Thus, although the spectrum has bands at 214 and 241 mμ, typical of αβ-unsaturated lactone and αβ-unsaturated ketone functions, respectively, it is apparent that these functions must be present in a cross-conjugated system since the molar extinction coefficients (7100 and 5000, respectively) are only about half the values associated with the separate functions, *i.e.*, β-cyclohexyl-$\Delta^{\alpha,\beta}$-butenolide and tetrahydromonascin have $\lambda_{max.}$ 212 (ε 15,000) and 244 mμ (ε 10,000), respectively.

The evidence already presented defines all the features of structure (III) for monascin apart from the angular methyl group. The location of this is based primarily on deductions from nuclear magnetic resonance spectra which, incidentally, provide strong confirmatory evidence for the complete structure (see Appendix). However, some chemical evidence has been obtained for the position of this methyl group. Thus, treatment of tetrahydromonascin with barium hydroxide and acidification of the reaction mixture gave a non-acidic gum, which showed bands at 3448, 1709, and 1667 cm.$^{-1}$ in its infrared spectrum. The absence of absorption at 1770 cm.$^{-1}$ suggested that this product was essentially the α-ketol (XVI) arising from tetrahydromonascin by hydrolysis of the γ-lactone function with subsequent

[13] Holker, Powell, Robertson, Simes, and Wright, *J.*, 1953, 2414.
[14] Personal communication from Professor B. Lythgoe, F.R.S.
[15] Paist, Blout, Uhle, and Elderfield, *J. Org. Chem.*, 1941, **6**, 273.

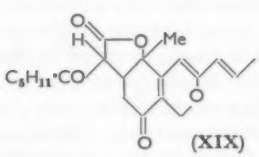
XUM

decarboxylation of the resultant β-keto-acid. In keeping with structure (XVI), the product reacted with lead tetra-acetate to give an acidic gum, which, unlike tetrahydromonascin, gave a positive iodoform reaction. Hence this acidic oxidation product apparently contained a methyl ketone function, in agreement with the position of the angular methyl group in the monascin structure.

Since the suggested structures for monascin and its hydrogenated derivatives contain a β-keto-lactone system having one hydrogen on the α-carbon atom, the absence of enolic properties in these compounds must be considered. In this connection it is known that no enolic properties are shown by compounds containing β-keto-ester systems in which the generation of an enol is sterically or energetically unfavourable, *e.g.*, compound (XVII).[16] Since there do not appear to be any adverse steric factors in structure (III) for monascin, it seems likely that energetic factors operate, *e.g.*, if the γ-lactone ring in this structure is *trans*-fused, the generation of an enol would be energetically unfavourable. There is some evidence that tetrahydromonascin (VI) does form an enol acetate. Thus, treatment of this compound with acetic anhydride and pyridine gave an amorphous product which regenerated compound (VI) on hydrolysis with dilute sodium hydroxide. The infrared spectrum of the amorphous product, which showed no absorption attributable to a saturated ketone function, is in agreement with the enol acetate structure. Acetylation of the dilactone (XIII) gave a crystalline monoacetate which was reconverted into the parent by hydrolysis. This acetate is tentatively formulated as (XVIII) despite the presence in its infrared spectrum of a band at 1724 cm.$^{-1}$ which is best attributed to a saturated carbonyl function. This band may well be due to the cyclic ketone group in structure (XVIII), since it is known from ultraviolet data that the corresponding group in the dilactone (XIII) is not fully conjugated with the αβ-double bond.

Finally, in view of the co-occurrence of monascin and "monascorubrin" in *M. purpureus*, and since the latter substance is known to be a mixture of rubropunctatin (I) and the higher homologue monascorubrin (II), it seemed likely that monascin from this source might also be a similar mixture of compounds (III) and (V). Comparative mass spectrometric examination of tetrahydromonascin samples derived from *M. purpureus* and *rubropunctatus* has shown no molecular ions of *m/e* greater than 362 [corresponding to structure (III)] but, in view of the extensive fragmentation under the experimental conditions, the possibility cannot be discounted that small amounts (<15%) of a homologue of type (V) are present in one or both samples. To test this hypothesis further, samples of monascin derived from both fungi have been oxidised with potassium permanganate and the steam-volatile acids products isolated. Paper chromatographic examination has revealed in each case a major spot due to hexanoic acid (which has been independently characterised as the *p*-bromophenacyl ester [8]) and a trace of a minor spot of higher R_F value which may be due to octanoic acid arising from a compound of structure type (V). However, since a compound of this type must be present in very minor amounts, and in any case would be difficult to separate, it has been ignored in the present studies.

[*Added in proof.* After submission of this paper structure (XIX) was proposed [20] for monascin (monascoflavin). In the absence of experimental detail in the Japanese paper we are unable to assess the evidence for this structure. However, in our opinion the production of iodoform by successive reaction of tetrahydromonascin with barium hydroxide, lead tetra-acetate, and iodine in sodium hydroxide is difficult to reconcile with structure (XIX) for monascin. Further, the formation of tetrahydroapomonascin from tetrahydromonascin under very mild reductive conditions, together with the infrared spectral data for hexahydromonascin, are not readily explicable in terms of structure (XIX).]



(XIX)

[16] Sondheimer, Mechoulam, and Sprecher, *Tetrahedron Letters*, 1960, No. 22, 38.

Appendix

Nuclear Magnetic Resonance Spectra of Monascin and its Derivatives.

By L. M. Jackman, Chemistry Department, Imperial College of Science and Technology

The spectra of monascin (III), dihydro- (IV), tetrahydro- (VI), and tetrahydroapomonascin (VIII) were determined at 56·4 Mc./sec. for solutions in deuterochloroform. The spectrum of monascin exhibits a complex band between 3·0 (τ) and 4·0 which undoubtedly arises from the olefinic protons of the disubstituted double bond. These protons, together with the three protons of the methyl group on the double bond, constitute an ABX_3 nuclear spin system. A detailed analysis was not attempted since it could be shown by a double irradiation technique * that a strong doublet at 8·14 (olefinic methyl) corresponded to the X_3 absorption of the ABX_3 system. By using the same technique it was possible to simplify the complex AB region to an isolated AB pattern from which the coupling constant ($J = 15$ c./sec.) between the olefinic protons could be determined. The magnitude of this coupling constant establishes a *trans*-configuration for the double bond. All lines of the ABX_3 system were absent from the spectra of the above derivatives of monascin. The olefinic region of the spectrum of monascin also contained a singlet at 4·40. This band was found at a higher frequency (4·76) in dihydromonascin but was absent from the spectra of compounds (VI) and (VIII). The diamagnetic shift of this absorption, which accompanies hydrogenation of the disubstituted double bond shows that the di- and tri-substituted double bonds are directly conjugated,[17] thus establishing the partial structure $\cdot CH{=}\overset{|}{C}\cdot CH{=}CH\cdot CH_3$.

The spectra of both monascin and dihydromonascin exhibit an AB system near 5·2 ($\tau_A = 4{\cdot}97$, $\tau_B = 5{\cdot}27$, $J = 12{\cdot}9$ c./sec., and $\tau_A = 5{\cdot}01$, $\tau_B = 5{\cdot}31$, $J = 12{\cdot}9$ c./sec., respectively). The positions of these bands are consistent with absorption arising from a methylene group which is both allylic and oxygenated,[17] and the coupling constant has the value expected for two protons attached to the same sp^3-hydridised carbon atom. The same band is present in the spectra of compounds (VI) and (VIII) but in both cases it is displaced by 0·40 p.p.m. to higher frequencies. This diamagnetic shift is expected, since hydrogenation of the central double bond of the triene system increases the electron density at the ether oxygen atom. The widths of the lines of the AB system suggest that the methylene protons are weakly coupled with other allylic protons.

A very sharp doublet is observed near 6·09 in the spectra of compounds (III), (IV), and (VI), but not in (VIII). This band must therefore arise from the single proton of the β-keto-lactone system. The coupling constant ($J = 12{\cdot}5$ c./sec.) is large and suggests that this proton is coplanar with and probably *cis* to that at the angular position between the lactone and the carbocyclic ring.[17] Another feature common to the spectra of (III), (IV), and (VI), but absent from that of (VIII) is a strong, sharp singlet at 8·50 which must arise from a methyl group at a fully substituted carbon atom. Its position is that expected for a methyl group attached to the same carbon atom as a carbonyl group and an oxygen atom.[17]

The fact that all the well-defined features of the complex spectra of monascin and its derivatives can be accommodated by structure (III) provides strong supporting evidence for it.

* A refined technique for the double irradiation of protons has been developed by Dr. D. W. Turner and details of the method will shortly be published.

[17] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, London, 1959.

XUM

Experimental

Unless otherwise stated, ultraviolet absorption spectra were measured for 95% alcohol solutions with a Unicam S.P. 500 spectrophotometer, infrared spectra for chloroform solutions with a Perkin-Elmer model 21 instrument, and optical rotations for chloroform solutions at room temperature (17—21°).

Monascin (III) *and "Monascorubrin" from* Monascus purpureus *Went.*—A culture of this organism, obtained from the Centraal-bureau voor Schimmelcultures, Baarn, Holland, was grown on the medium described by Nishikawa [5] at 30° for 21—28 days until pigmentation was complete. Maceration of the undried red mycelial mats with cold ether was continued until the extract was no longer highly coloured. The crude pigment, isolated by concentration of the extract, was resolved by fractional crystallisation from ether into "monascorubrin," red needles (from ether), m. p. 134—136° (decomp.), "monascorubramine," purple needles (from benzene), m. p. 198° (decomp.), and monascin, yellow needles (from ether or alcohol), m. p. 142—144° (decomp.), $[\alpha]_D$ +544° (*c* 1·27), $\lambda_{max.}$ 231, 287, and 390 mμ (log ε 4·18, 3·60, and 4·21) (Found: C, 70·7; H, 7·5; *C*-Me, 10·5; active H, 0·25; OMe, 0. Calc. for $C_{21}H_{26}O_5$: C, 70·4; H, 7·3; 3*C*-Me, 12·2; 1 active H, 0·28%). In an alternative procedure for the separation of monascin, the pigment mixture (3 g.) in ether (1 l.) was shaken with aqueous ammonia (*d* 0·88) (18 ml.) in water (750 ml.). After addition of concentrated hydrochloric acid (25 ml.), the ether layer was separated, dried (Na_2SO_4), and evaporated. The residue in benzene (250 ml.) was chromatographed on a column (12 in. × 1 in.) of silica gel. Elution with benzene–ether (9 : 1) gave monascin (1·8 g.), and benzene–acetone (1 : 1) gave "monascorubramine" (0·5 g.). When separated in this way, the pigment obtained from 500 penicillin flasks, each containing 250 ml. of culture medium, gave approximately 40 g. of monascin and 10 g. of "monascorubramine."

Further concentration of the ether extract from the mycelium gave a white solid which was resolved by fractional crystallisation from ether into ergosterol, needles (from methanol), m. p. and mixed m. p. 161° (*O*-acetate, m. p. and mixed m. p. 171°), and stearic acid, needles (from light petroleum), m. p. and mixed m. p. 68° (amide, m. p. and mixed m. p. 106°).

Monascin and Rubropunctatin (I) *from* M. rubropunctatus *Satô.*—When grown on Czapek–Dox solution [18] as previously described,[1a] this organism gave monascin, m. p. 142—144° (decomp.) (Found: C, 70·6; H, 7·5%), and rubropunctatin, m. p. 156—157° (decomp.) (Found: C, 71·2; H, 6·3. Calc. for $C_{21}H_{22}O_5$: C, 71·2; H, 6·3%).

Monascin from M. rubiginosus *Satô.*—This organism, obtained from the Centraal-bureau voor Schimmelcultures, Baarn, Holland, was grown at 30° for 28 days in 390 penicillin flasks, each containing Nishikawa's solution [5] (500 ml.). The dried, milled mycelium (1000 g.) was percolated with light petroleum (b. p. 60—80°) and the extract concentrated (to 500 ml.). Monascin, which separated on cooling, was crystallised from ether, giving yellow needles (4·3 g.), m. p. and mixed m. p. 142—143° (decomp.). Further concentration (to 300 ml.) of the light-petroleum extract gave ergosterol, plates (from methanol), m. p. and mixed m. p. 158—161°, $[\alpha]_D$ −127° (*c* 1·13) [*O*-acetate, plates (from methanol–ether), m. p. and mixed m. p. 173—174°].

Monascin was extracted from ether with 2N-sodium hydroxide and was reprecipitated from the alkaline solution with carbon dioxide. The pigment gave a positive hydroxamic acid test, a negative iodoform reaction, developed no colour in the Legal test,[15] and did not reduce Fehling's or Tollens's reagent.

Dihydromonascin (IV).—Hydrogenation of monascin (1·0 g.) in alcohol (100 ml.) at atmospheric pressure with 5% palladium–barium sulphate (500 mg.) was complete in 1 hr., and 1 mol. of gas had then been absorbed. On isolation, *dihydromonascin* separated from aqueous alcohol in pale yellow needles (950 mg.), m. p. 119—121° (decomp.), $[\alpha]_D$ +445° (*c* 1·01), $\lambda_{max.}$ 248 and 365 mμ (log ε 3·60 and 4·18) (Found: C, 70·2; H, 8·0; active H, 0·25. $C_{21}H_{28}O_5$ requires C, 70·0; H, 7·8; 1 active H, 0·28%).

Tetrahydromonascin (VI).—Hydrogenation of monascin (1·0 g.) in alcohol (200 ml.) at atmospheric pressure in the presence of 10% palladium–carbon (500 mg.) was terminated after 2·2 mol. of gas had been absorbed (*ca.* 1 hr.). The filtered solution was concentrated (to 15 ml.) and diluted with a few drops of water. On cooling, a colourless solid separated; it was recrystallised from aqueous alcohol giving *tetrahydromonascin* (500—650 mg.) as needles, m. p.

[18] Raistrick and Rintoul, *Phil. Trans.*, 1931, *B*, **220**, 2.

135°, $[\alpha]_D$ +245° (*c* 1·02) [Found: C, 69·5; H, 8·2; active H, 0·29%; *M* (mass spectrometry), 362. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·3; 1 active H, 0·27%; *M*, 362]. The same compound (500—650 mg.) was also prepared from dihydromonascin (1·0 g.) by a similar procedure, the reaction being terminated after absorption of 1·1 mol. of gas.

Acetylation of tetrahydromonascin (200 mg.) with acetic anhydride (3 ml.) and pyridine (1 ml.) at room temperature for 15 hr., and isolation of the product in ether in the usual way, gave a gum (189 mg.), $\nu_{max.}$ 1770s and 1689s cm.$^{-1}$. On treatment with 2N-sodium hydroxide (15 ml.) for 15 min., this material (180 mg.) in methanol (5 ml.) regenerated tetrahydromonascin (130 mg.), needles (from aqueous alcohol), m. p. and mixed m. p. 135°.

Hexahydromonascin (VII).—Hydrogenation of tetrahydromonascin (200 mg.) in alcohol (30 ml.) at atmospheric pressure in the presence of 10% palladium–carbon (100 mg.) was terminated after 1·1 mol. of gas had been absorbed. Concentration of the filtered solution gave *hexahydromonascin* as fine needles (60 mg.), m. p. 208—209°, $[\alpha]_D$ +75° (*c* 1·00) (Found: C, 69·0; H, 8·7; active H, 0·28. $C_{21}H_{32}O_5$ requires C, 69·2; H, 8·8; 1 active H, 0·27%). This experiment was difficult to reproduce, the reaction time and yield varying with each batch of catalyst.

Hexahydromonascin, in ethanol, slowly absorbed hydrogen (*ca.* 1 mol.) at atmospheric pressure in the presence of 10% palladium–carbon to give a glass, $\nu_{max.}$ 3500m, 1786s, and 1718m cm.$^{-1}$.

Ozonolysis of Monascin and its Dihydro-derivative.—(*a*) *In ethyl acetate.* A stream of ozone and oxygen was led into a solution of monascin (400 mg.) in ethyl acetate (30 ml.) at −70° until absorption was complete (*ca.* 2 hr.). The pale yellow solution was evaporated *in vacuo*, and the residue treated with water (15 ml.) for 15 hr. at room temperature. After removal of the insoluble material, acetaldehyde was isolated from the aqueous solution in steam and characterised as the 2,4-dinitrophenylhydrazone (120 mg., 48%), yellow blades (from alcohol), m. p. and mixed m. p. 164—166°. Ozonolysis of dihydromonascin (500 mg.) under similar conditions gave no volatile aldehydic or ketonic product.

(*b*) *In carbon tetrachloride.* Monascin (400 mg.), in carbon tetrachloride (150 mg.), was treated with ozone and oxygen at room temperature until the yellow colour of the solution was discharged (4 hr.). After removal of the solvent under reduced pressure and decomposition of the residual ozonide with zinc dust (1 g.) and water (25 ml.) at room temperature for 12 hr., acetaldehyde was isolated from the reaction mixture by distillation in methanol, and characterised as the 2,4-dinitrophenylhydrazone (90 mg., 36%; m. p. 165—166°). The aqueous phase (after distillation with methanol) was distilled in steam into a solution of 2,4-dinitrophenylhydrazine hydrochloride. The resultant deep orange precipitate (20 mg.) was adsorbed on neutral alumina from solution in benzene. Chloroform–benzene (1 : 1) eluted a sticky red solid (15 mg.), m. p. 280—290°, which could not be purified further. The infrared spectrum (in mineral oil dispersion) was very similar to that of authentic pyruvaldehyde 2,4-dinitrophenylosazone, m. p. 300° (decomp.). Ozonolysis of dihydromonascin under parallel conditions gave no volatile aldehydic or ketonic product.

Tetrahydroapomonascin (VIII).—Zinc dust (8 g.) was added in one portion to a vigorously stirred solution of tetrahydromonascin (1 g.) and anhydrous sodium acetate (2 g.) in acetic acid (50 ml.) at room temperature. After 1 hr. more zinc dust (2 g.) was added and stirring continued for a further 1 hr. Carbon dioxide evolved during the reaction was estimated as barium carbonate (Found: 240 mg. of $BaCO_3$. 1 CO_2 corresponding to 400 mg. of tetrahydroapomonascin requires 300 mg. of $BaCO_3$). After filtration, the original reaction mixture was concentrated (to 10 ml.), diluted with water (50 ml.), and extracted with ether (3 × 80 ml.). The ether extract was washed in turn with 2N-sodium hydroxide (5 × 50 ml.) and water (3 × 50 ml.), dried (Na_2SO_4), and evaporated. The residual gum was crystallised from light petroleum (b. p. 60—80°) giving *tetrahydroapomonascin* as long needles (400 mg.), m. p. 102°, $[\alpha]_D$ +175° (*c* 1·00), $\lambda_{max.}$ 243 mμ (log ε 4·03) (Found: C, 75·1; H, 10·2; *C*-Me, 11·8. $C_{20}H_{32}O_3$ requires C, 75·0; H, 10·0; 3*C*-Me, 14·1%). Acidification (HCl) of the 2N-sodium hydroxide washings gave a buff-coloured solid which separated from methanol as fine needles (30 mg.) of hexahydromonascin, m. p. and mixed m. p. 208—209°.

Reduction of monascin (500 mg.) in ethanol (10 ml.) and acetic acid (25 ml.) with zinc dust (5 g.) under similar conditions gave carbon dioxide (Found: 80 mg. of $BaCO_3$; 1 CO_2 from 500 mg. of monascin requires 276 mg. of $BaCO_3$). Partition of the residue in the usual way gave " neutral " (200 mg.) and " acidic " (200 mg.) fractions which could not be crystallised.

Under similar conditions hexahydromonascin (100 mg.) gave only unchanged starting material (92 mg.), m. p. and mixed m. p. 208—209°, and no carbon dioxide could be detected.

Oxidation of Dihydromonascin with Sodium Dichromate.—Solutions of dihydromonascin (1 g.) in acetic acid (40 ml.) and sodium dichromate (2·5 g.) in water (10 ml.) were mixed and kept at room temperature for 15 hr. The reaction mixture was diluted with water (50 ml.) and poured into an excess of 2N-sodium hydrogen carbonate (*ca.* 1 l.). Isolated in ether and crystallised from benzene, the *formyl-butyrate* (XI) formed small needles (400 mg.), m. p. 183° (decomp.), $[\alpha]_D$ +212° (*c* 1·00); $\nu_{max.}$ 1789s (γ-lactone), 1742sh ($CO_2C_3H_7$), 1718s (saturated ketone), and 1684s cm.$^{-1}$ (O=C·C=C·CHO) (Found: C, 64·4; H, 7·5; *C*-Me, 7·90. $C_{21}H_{28}O_7$ requires C, 64·2; H, 7·2; 3*C*-Me, 11·5%). The sodium hydrogen carbonate solution was acidified with concentrated hydrochloric acid and extracted with ether (5 × 50 ml.), and the extract evaporated. On treatment of the residue with water (50 ml.) a precipitate was obtained which was crystallised from ice-cold ether giving the *monohydrate* of the acid ester (XII) as micro-needles (200 mg.), m. p. 143° (decomp.), $[\alpha]_D$ + 144° (*c* 1·00); $\lambda_{max.}$ 242 mμ (log ε 3·85); $\nu_{max.}$ (mineral oil dispersion) 3367(m + b) (hydrate), 2618(w + b) (·CO_2H), 1786s (γ-lactone), 1736sh (·$CO_2C_3H_7$), 1718s (saturated ketone), 1701sh (·CO_2H) and 1689sh cm.$^{-1}$ (sh) (O=C·C=C·CO_2H) (Found: C, 59·1; H, 7·1; *C*-Me, 9·7. $C_{21}H_{28}O_8,H_2O$ requires C, 59·0; H, 7·0; 3*C*-Me, 10·5%). Evaporation of this hydrate with benzene gave the *anhydrous acid* (Found: C, 61·0; H, 6·9. $C_{21}H_{28}O_8$ requires C, 61·8; H, 6·9%).

Compounds (XI) and (XII) reduced Tollens's and Fehling's reagents. The aldehyde (XI) reacted immediately with an alcoholic solution of 2,4-dinitrophenylhydrazine sulphate to give a *mono-2,4-dinitrophenylhydrazone*, orange needles, m. p. 270° (decomp.) (Found: N, 9·4. $C_{27}H_{32}O_{10}N_4$ requires N, 9·8%). The acid (XII) reacted slowly with the same reagent giving an amorphous orange solid. Treatment of the acid (XII) with diazomethane in ether gave a glass; $\nu_{max.}$ 1786s, 1739s, 1724s, and 1709sh cm.$^{-1}$.

Oxidation of the aldehyde (XI) (500 mg.) with sodium dichromate (1·2 g.), as described for dihydromonascin, gave the monohydrate of the acid (XII) (200 mg.), m. p. and mixed m. p. 143° (decomp.), and unchanged aldehyde (XI) (150 mg.), m. p. and mixed m. p. 183° (decomp.).

The Dilactone (XIII).—(*a*) To monascin (1 g.) in acetone (40 ml.) at room temperature was added, dropwise, a solution (*ca.* 4 ml.) of chromium trioxide (13·5 g.) in sulphuric acid (11·5 ml.) and water (25 ml.) until the red-brown colour due to excess oxidising agent persisted for 10 min. The reaction mixture was then diluted with water (100 ml.) and extracted with ether (4 × 100 ml.) and the ether solution partitioned with saturated sodium hydrogen carbonate solution (5 × 80 ml.) and 2N-sodium hydroxide (5 × 40 ml.) into "neutral" (trace), "acidic" (850 mg. of intractable brown gum), and "enolic" (120 mg. of pale yellow solid) fractions. A solution of the "enolic" fraction in benzene (30 ml.) was chromatographed on silica gel (15 × 1 cm.). Chloroform–benzene (1 : 1) eluted the *dilactone* (XIII), which separated from benzene as small needles (100 mg.), m. p. 188°, $[\alpha]_D$ +222° (*c* 1·00), $\nu_{max.}$ 1789s (saturated γ-lactone), 1770s (αβ-unsaturated γ-lactone), 1721s (saturated ketone), and 1692m, sh cm.$^{-1}$ (αβ-unsaturated ketone) (Found: C, 63·7; H, 6·6; active H, 0·64; *C*-Me, 8·5. $C_{17}H_{20}O_6$ requires C, 63·7; H, 6·3; 2 active H, 0·63; 2*C*-Me, 9·3%).

(*b*) Oxidation of dihydromonascin (1 g.) by the above procedure gave an intractable "acid" fraction (850 mg.) and the dilactone (XIII), needles (85 mg.), m. p. and mixed m. p. 188°, from benzene. Under similar conditions, oxidation of tetrahydromonascin (500 mg.) gave an intractable acid fraction (40 mg.) and unchanged starting material, needles (420 mg.), m. p. and mixed m. p. 135°, from aqueous alcohol.

(*c*) The acid (XII) (500 mg.) was dissolved in 2N-sodium hydroxide (10 ml.) and, after 3 min. at room temperature, the solution was acidified with 2N-sulphuric acid. n-Butyric acid was separated in steam, isolated as its sodium salt, and converted, in the usual way, into the anilide which formed long needles (130 mg.), m. p. and mixed m. p. 95°, from light petroleum (b. p. 60—80°) (Found: C, 74·0; H, 8·4; N, 8·7. Calc. for $C_{10}H_{13}NO$: C, 73·6; H, 8·0; N, 8·6%). The dilactone (XIII), which was isolated in ether from the residue after steam distillation, separated from benzene in needles (320 mg.), m. p. and mixed m. p. 188°. Hydrolysis of the aldehyde (XI) (400 mg.), under similar conditions, gave n-butyric acid [characterised as the anilide (100 mg.), m. p. and mixed m. p. 95°] and an intractable brown gum (250 mg.).

(*d*) Treatment of the glassy methyl ester of acid (XII) (50 mg.) with methanol (0·2 ml.)

XUM

and 2N-sodium hydroxide (1 ml.) for 10 min. at room temperature, followed by acidification, gave the dilactone (XIII), small needles (23 mg.), m. p. and mixed m. p. 188°, from benzene.

The dilactone (XIII) reduced Fehling's and Tollens's reagents but did not give a ferric test or an iodoform reaction. Prepared with acetic anhydride and pyridine, the *monoacetate* (XVIII) separated from methanol in needles, m. p. 212°; $\lambda_{max.}$ 218 and *ca.* 240 infl. mμ (log ε 4·26 and 4·03); $\nu_{max.}$ 1779—1767(vs + b), 1727s, 1689m, and 1157s cm.$^{-1}$ (Found: C, 63·1; H, 6·4; active H, 0·26; *O*-Ac, 14·8. $C_{19}H_{22}O_7$ requires C, 63·0; H, 6·1; 1 active H, 0·27; 1 *O*-Ac, 12·0%). This compound (100 mg.), moistened with methanol (0·5 ml.), dissolved slowly in 2N-sodium hydroxide. Acidification gave the parent dilactone (80 mg.), m. p. and mixed m. p. 188°.

On reduction of the dilactone (XIII) with zinc and acetic acid at room temperature, carbon dioxide was produced in about the same molar proportion as from monascin under similar conditions.

Degradation of Tetrahydromonascin with Barium Hydroxide.—Tetrahydromonascin (500 mg.) in methanol (10 ml.) and a saturated solution of barium hydroxide in water (100 ml.) were heated together, for 1 hr., under reflux in an atmosphere of nitrogen. After acidification of the boiling solution with concentrated hydrochloric acid, the mixture was extracted with ether and the ether solution washed with 2N-sodium hydroxide (3 × 50 ml.) and water (50 ml.), and dried (Na_2SO_4). Evaporation of the ether left a colourless gum (380 mg.); $\nu_{max.}$ 3448m, 1709s, and 1667s cm.$^{-1}$. This material (100 mg.) in acetic acid (8 ml.) and water (2 ml.) was oxidised with finely powdered lead tetra-acetate (150 mg.) for 15 min. at room temperature. After dilution of the mixture with water (30 ml.), the product was separated in ether (3 × 20 ml.), extracted with saturated sodium hydrogen carbonate solution (3 × 20 ml.), and after acidification of this solution, re-extracted into ether (3 × 20 ml.). To a solution of this acidic material in 2N-sodium hydroxide (1 ml.) were added, dropwise, iodine (1 g.) and potassium iodide (2 g.) in water (4 ml.) until a brown colour due to excess of iodine persisted for 5 min. This colour was removed with a few drops of 2N-sodium hydroxide and the mixture diluted with water (50 ml.); iodoform (40 mg. 33% of calc. amount) separated, m. p. and mixed m. p. 118°.

Oxidation of Monascin and the Dilactone (XIII) *with Potassium Permanganate.*—Potassium permanganate (1 g.) in water (50 ml.) was added dropwise during ½ hr. to a boiling solution of monascin (200 mg.), moistened with methanol (0·5 ml.), in 2N-sodium hydroxide (25 ml.). The reaction mixture was acidified with dilute sulphuric acid, clarified with sulphur dioxide, and then distilled in a current of steam. The volatile acids were isolated in ether and a small amount of this solution was spotted on to a strip of filter paper ("Whatman" No. 1). Hexanoic and octanoic acid were also separately spotted on to the same paper, which was then exposed to ammonia gas to convert the acids into their ammonium salts. On chromatography of these salts with butanol–1·5N-ammonium hydroxide (1 : 1) as the mobile phase,[19] and the development of the paper with Bromothymol Blue, the mixed degradation acids separated into a large spot and a small spot, having R_F values identical with those of ammonium hexanoate (R_F 0·61) and octanoate (R_F 0·74), respectively.

Oxidation of the dilactone (XIII) under parallel conditions gave similar results.

The authors are indebted to Professor B. Lythgoe, F.R.S., for helpful discussions and information in advance of publication, Dr. J. B. Matthews of the Thornton Research Centre, Shell Refining Co. Ltd., for arranging the mass-spectral determination, and Mr. A. Quayle for performing these measurements and interpreting the results. They also thank the Department of Scientific and Industrial Research and Messrs. Goodlass Wall and Co. Ltd. for Maintenance Grants (to D. F. J. and A. D. G. P., respectively).

UNIVERSITY OF LIVERPOOL. [*Received, March 8th,* 1961.]

[19] Reid and Lederer, *Biochem. J.*, 1951, **50**, 60.
[20] Ohashi, Yamamura, Terahara, and Nakanishi, *Bull. Chem. Soc. Japan*, 1960, **33**, 1630.

899. *The Structure of Complex Molybdenum(III) Thiocyanates.*

By J. Lewis, R. S. Nyholm, and P. W. Smith.

The nature of the metal–ligand bond in molybdenum(III) thiocyanate complexes has been investigated. The infrared spectra of a number of transition-metal thiocyanates and isothiocyanates of the types $[M(CNS)_6]^{n-}$ and $[M(CNS)_4]^{n-}$ have been studied: the feature most characteristic of metal–sulphur bonding is a lower C–S stretching frequency, ~700 cm.$^{-1}$, to be compared with ~800 cm.$^{-1}$ when the bonding is to the nitrogen atom. This leads to the conclusion that the $[Mo(CNS)_6]^{3-}$ complexes are isothiocyanates. Additional evidence in favour of this formulation is provided by *X*-ray isomorphism and visible and ultraviolet spectra. The role of the water molecules in the hydrated $[Mo(NCS)_6]^{3-}$ complexes is discussed and it is concluded that they are not co-ordinated to the metal atom. Magnetic data on a number of tervalent molybdenum complexes are reported. In all cases except $K_4Mo(CN)_7,2H_2O$ the magnetic moments correspond to the presence of three unpaired electrons and hence to six-co-ordination. For the complex cyanide the moment is 1·75 B.M. and the molybdenum atom is considered to be seven-co-ordinate. Finally, factors which are important in deciding whether a metal atom will bond to sulphur or nitrogen in $[NCS]^-$ are discussed briefly and an explanation is proposed.

The hexathiocyanatomolybdenum(III) * complexes have been of interest, partly because of the doubt expressed in some quarters as to whether the Mo(III) atom is really six-co-ordinate therein and partly because of the uncertainty as to the way in which the (CNS) group is attached to the metal atom.

As discussed by Lindqvist and Strandberg,[1] the transition metals may be classified into two groups according to whether they are bonded to the thiocyanate group through the nitrogen or sulphur atom. Thus, metals in the first transition series appear to form isothiocyanate complexes (N-bonded), whereas elements in the second half of the second and third transition series tend to form thiocyanates (S-bonded). It is significant that this behaviour closely parallels the division into class (*a*) and class (*b*) acceptors proposed recently by Ahrland, Chatt, and Davies [2] for the co-ordination of metal ions with an extensive series of ligands. This (*a*)–(*b*) division is based upon the stability constants of ions in solution, *i.e.*, the free energies of replacement of one ligand by another. For class (*a*) metals the order of strength of attachment in water is $F^- > Cl^- > Br^- > I^-$ and for class (*b*) metals the order is reversed. The behaviour of molybdenum is of particular interest since it has been assigned a border-line position. In the case of the thiocyanate complexes no *X*-ray data are available to establish whether it is nitrogen or sulphur which is bound to molybdenum, but we have been able to obtain information by other physical methods. The fact that the bonding extremes are M–N=C=S and M–S–C≡N on conventional formulation suggested that it should be possible to distinguish between the two forms by studying the CN and CS frequencies in the infrared spectrum. In addition we have investigated the visible spectra of these complexes with a view to correlating the different ways in which bonding can occur with the difference in position of –SCN and –NCS in the spectrochemical series. The positions of the latter have been demonstrated by Yamada and Tsuchida [3] and more recently by Schäffer.[4]

The second aspect of interest arises from recent evidence that the well-known tendency

* "Thiocyanate" and (CNS) are used without prejudice as to whether the group is sulphur- or nitrogen-bonded to a metal atom.

[1] Lindqvist and Strandberg, *Acta Cryst.*, 1957, **10**, 176.
[2] Ahrland, Chatt, and Davies, *Quart. Rev.*, 1958, **12**, 265.
[3] Yamada and Tsuchida, *Bull. Chem. Soc. Japan*, 1953, **26**, 492.
[4] Schäffer, Internat. Conf. Co-ordination Chemistry, *Chem. Soc. Special Publ.*, 1959, No. 13, p. 153.

of molybdenum to exhibit co-ordination numbers greater than 6 when quadri-, quinque-, and sexi-valent extends also to the lower oxidation states. Recently seven-co-ordinate molybdenum(II) has been shown to occur in compounds of the type $[Mo(Diarsine)(CO)_3X_2]^0$ where X = I or Br; these complexes are monomeric and non-electrolytes in suitable organic solvents such as nitrobenzene.[5] The well-known heptacyanomolybdate(III) ion [6] has also been considered for some time to be an example of seven-co-ordinate molybdenum(III). Unlike the complex molybdenum(III) thiocyanates, however, in both of these classes of compound spin pairing occurs, as will be discussed below.

These facts revive interest in the question whether a co-ordination number of seven should be assigned to the hydrated hexathiocyanate complexes of molybdenum(III). The ammonium and potassium salts, for example, crystallise as yellow tetrahydrates but there has been some controversy as to whether the complex ions should be formulated as $[Mo(CNS)_6]^{3-}$ (ref. 7) or $[Mo(CNS)_6(H_2O)]^{3-}$ (ref. 8); the difference in viewpoint is based upon conflicting evidence on the retention of one molecule of water in the potassium and ammonium salts when dehydration occurs. We have observed that, although it is possible to prepare the anhydrous potassium salt, in the case of the ammonium salt the final product of " dehydration " under a vacuum is the monohydrate, as previously reported. Further apparent evidence for the assignment of a co-ordination number exceeding six is the formation of a series of addition compounds involving one molecule of water and an organic molecule to give compounds of the formula $M^I_3Mo(CNS)_6,H_2O,HA$, where HA = hydrochloric acid, acetic acid, potassium hydrogen oxalate, or ethyl or propyl alcohol. Most of these compounds appear to be more stable in air and less soluble in water than the parent hydrates. For the hydrogen chloride and ethyl alcohol adducts of the ammonium salt, we have found that the alcohol and hydrogen chloride are lost readily in a vacuum, leaving the monohydrate. However, we have been unable to detect the presence of a hydrogen–chlorine stretching frequency in the infrared spectrum of the hydrogen chloride adduct and this suggests that this complex is not simply an addition compound of hydrogen chloride and the metal complex.

Although a co-ordination number of seven is certainly possible for molybdenum(III) complexes, evidence for this based solely on the facility with which a molecule of water is retained in the complex is by no means conclusive. In an attempt to determine the co-ordination number of molybdenum in these complexes we have investigated the magnetic properties of a series of compounds. This follows recent work which has led to a better understanding of the magnetic properties of the second- and third-row transition elements. If the hexathiocyanates are formulated as six-co-ordinate complexes, the molybdenum ion would have a configuration d_ϵ^3; in a perfect cubic crystal field this would split, to give an orbital singlet at the lowest level, and hence to a first-order approximation the magnetic moment would be expected to correspond to the spin-only value for three unpaired electrons (3·88 B.M.). However, spin–orbit coupling will mix in to this lowest singlet level some higher levels with orbital angular momentum, and as shown by Penny and Schlapp, the observed magnetic moment will then be given by

$$\mu_{obs} = \mu_{spin\text{-}only}\left(1 - \frac{4\lambda}{10Dq}\right)$$

where λ is the spin–orbit coupling constant for the set of *d*-electrons, and Dq is the crystal-field splitting parameter. For molybdenum(III), λ is 267 cm.$^{-1}$ for the free ion and $10Dq$ will be of the order 20,000 cm.$^{-1}$; the former will be reduced a little by complex formation, but the expected moment is of the order of 3·7 B.M. and, as the magnetic moment will be independent of temperature, the susceptibility should obey a Curie law.

[5] Nigam, Nyholm, and Stiddard, *J.*, 1960, 806.
[6] Young, *J. Amer. Chem. Soc.*, 1932, **54**, 1402.
[7] Rosenheim, *Ber.*, 1909, **42**, 2295.
[8] Maas and Sand, *Ber.*, 1909, **42**, 2642.

In the case of a seven-co-ordinate complex such as $[Mo(CNS)_6(H_2O)]^{3-}$ the magnetic behaviour is not so clearly defined, but since the compounds $Mo(CO)_3(Diars)X_2$ are diamagnetic, the *d*-orbitals of the molybdenum must be split by the crystal field to give two low-lying *d*-orbitals separated from the next *d*-orbitals by energy greater than the electron-pairing energy. In the case of a seven-co-ordinate molybdenum(III) complex, this could involve one electron less and we should expect a moment corresponding to one unpaired electron. However, without a detailed analysis of the problem, it is not possible to say how the susceptibility would vary with temperature.

In agreement with this, the magnetic moment of the heptacyanomolybdate(III) complex indicates one unpaired electron (Table 1), but the susceptibility deviates from the Curie law near room temperature, whereas at low temperatures Curie law behaviour is observed (Fig. 1). For the other compounds cited in the Table, the magnetic properties

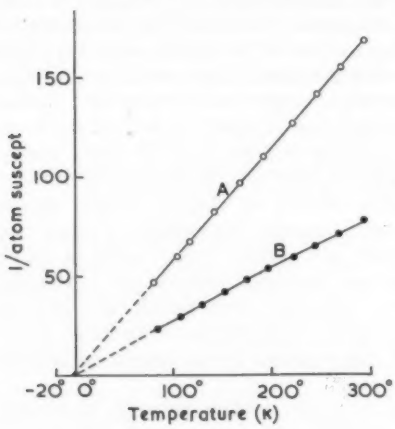


FIG. 1. Plot of the inverse of atomic susceptibility against temperature for (A) potassium hexathiocyanatomolybdate(III) and (B) heptacyanomolybdate(III).

are those expected for a six-co-ordinate complex. In the case of the potassium hexathiocyanatomolybdate(III) hydrate, the susceptibility differs little from that expected from the Curie law; θ is 3° in the Curie–Weiss equation, $\chi_A(T + \theta) = \text{Constant}$. Thus, the magnetic properties appear to favour a co-ordination number of six for these complexes.

TABLE 1.

Compound	μ_{eff} at 295° K	Compound	μ_{eff} at 295° K
K_3MoCl_6	3·79	$(NH_4)_3Mo(CNS)_6,HCl,H_2O$	3·70
$(NH_4)_3Mo(CNS)_6,4H_2O$	3·70	$K_3Mo(CNS)_6,4H_2O$	3·79
$(NH_4)_3Mo(CNS)_6,EtOH,H_2O$ ...	3·80	$K_4Mo(CN)_7,2H_2O$	1·75

We now come to the question of how the (CNS) group is attached to the metal atom. Since the shape and bond order within the group are expected to be affected by the mode of attachment, it is useful to summarise, at this stage, the *X*-ray structural data which are available on complexes in which (CNS) has a terminal position. These are given in Table 2.

It will be noted that only first-row transition elements form isothiocyanates and only the later second- and third-row transition metals form thiocyanates. In all cases the NCS group is linear. However, preliminary *X*-ray results [9] have been taken to indicate sulphur bonding in $K_4Ni(CNS)_6,4H_2O$ and $K_3Cr(CNS)_6,4H_2O$. This result for nickel(II) seems most unlikely in view of the more recent findings for the series of isothiocyanatoammines included in Table 2. Furthermore, sulphur bonding for chromium(III) is against chemical evidence. Seel,[10] for example, concluded that nitrogen bonding existed in

[9] Zvonkova, *Zhur. fiz. Khim.*, 1957, **31**, 2074.
[10] Seel, Co-ordination Chem. Conference, Copenhagen, 1953, p. 46; *Z. anorg. Chem.*, 1956, **283**, 351.

$K_3Cr(CNS)_6$, $K_2Co(CNS)_4$, and $NH_4[Cr(NH_3)_2(CNS)_4]$. Other structures have been reported in which the thiocyanate group serves to bridge two metal atoms, so increasing the co-ordination number of the metal. Examples of these compounds are: Co $py_2(NCS)_2$, $Ni(NH_3)_3(NCS)_2$, Cu $py_2(NCS)_2$, AgSCN, $[Pt_2\{P(C_3H_7)_3\}_2Cl_2(SCN)_2]$, $Hg(SCN)_4Co$, $Hg(SCN)_4Ni,2H_2O$. The infrared results reported below are, however, for compounds containing no bridging group.

TABLE 2.

X-Ray structures of thiocyanate complexes.

Compound	Stereochemistry of central atom	Arrangement of (CNS) groups in complex ion	Ref.
Isothiocyanates			
$[Cr(NH_3)_2(NCS)_4]^-$	Octahedral	Co-planar, M–NC co-linear	*a*
$[Co(NCS)_4]^{2-}$	Tetrahedral	Angular, ∠M–NC approx. 120°	*b*
$[Ni(NH_3)_2(NCS)_4]^{2-}$	Octahedral	Co-planar, M–NC co-linear	*c*
$[Ni(NH_3)_2(NCS)_2]^-$	Octahedral	M–NC co-linear	*c*, *d*
$[Ni(NH_3)_4(NCS)_2]$	Octahedral	*trans*-, M–NC co-linear	*c*
$[Ni\ py_4(NCS)_2]$	Octahedral	*trans*-, ∠M–NC 165°	*c*
$[Ni\ en_2(NCS)_2]$	Octahedral	*trans*-	*e*, *f*
[Ni tren $(NCS)_2$]	Octahedral	*cis*-, ∠M–NC 163°, 156°	*f*
Thiocyanates			
$[Rh(SCN)_6]^{3-}$	Distorted octahedral	–SCN groups parallel (in two sets) ∠M–SC 120°	*g*
$[Pt(SCN)_4]^{2-}$	Square planar	–SCN groups approx. parallel (in two sets)	*h*
$[Hg(SCN)_4]^{2-}$	Distorted tetrahedral	–SCN groups angular ∠M–SC 120°?	*i*
$[Ag(SCN)_2]^-$	Distorted tetrahedral	AgSCN and SCN^-, ∠Ag–SC 110°	*j*
$Pt(NH_3)_2(SCN)_2$ (*cis*- and *trans*-)	Square planar	–SCN angular	*k*

a, Saito, Takeuchi, and Pepinsky, *Z. Krist.*, 1955, **106**, 476; Takeuchi and Pepinsky, *ibid.*, 1957, **109**, 29; 1958, **110**, 474; Takeuchi and Saito, *Bull. Chem. Soc. Japan*, 1957, **30**, 319. *b*, Zhdanov and Zvonkova, *Zhur. fiz. Khim.*, 1950, **24**, 1339. *c*, Porai-Koshits, Iukhno, Antsishkina, and Dikareva, *Soviet Phys. Cryst.*, 1957, **2**, 366. *d*, Porai-Koshits, *Trudy Inst. Krist., Akad. Nauk S.S.S.R.*, 1954, **10**, 117. *e*, Lingafelter, *Nature*, 1958, **182**, 1730. *f*, Rasmussen, *Acta Chem. Scand.*, 1959, **13**, 2009. *g*, Zvonkova, *Zhur. fiz. Khim.*, 1953, **27**, 100. *h*, Zvonkova, *Zhur. fiz. Khim.*, 1952, **26**, 1804. *i*, Zvonkova, *Zhur. fiz. Khim.*, 1952, **26**, 1798. *j*, Lindqvist and Strandberg, *Acta Cryst.*, 1957, **10**, 173. *k*, Bleidelis, *Soviet Phys. Cryst.*, 1957, **2**, 270; Bleidelis and Bokii, *ibid.*, p. 274.

The infrared frequencies attributed to the vibrations of the thiocyanate group are listed in Table 3, the groupings being on the basis of the detailed assignments for KNCS,[11,12a] NH_4NCS,[12b] and HNCS.[13] No complete investigation of a thiocyanate complex of the type we have considered has been reported, except by Kinell and Strandberg [14] for AgSCN and $Ag(SCN)_2^-$. The band we ascribe to the C–S (symmetrical N–C–S) stretching vibration is often of low intensity and difficult to find when normal mull thicknesses are used but that it is clearly not an overtone is shown by examination of spectra at longer wavelengths. A similar difficulty has been reported in identifying C–S linkages in organic compounds.[15] Chamberlain and Bailar [16] have adopted the same assignment for a series of cobalt complexes. In connection with the assignment of the lowest frequencies to the bending modes, the possibility of a metal–nitrogen stretching frequency in the same region (500—400 $cm.^{-1}$) has to be considered. However, in the hexaisothiocyanates we have been able to detect one band system only; the general similarity of this to the band in the alkali-metal thiocyanates, along with other results, suggests that this stretching frequency must lie below 400 $cm.^{-1}$. Jones [11] has drawn attention to a remarkable feature of the KNCS spectrum, namely, that the first overtones of the bending frequencies are of about the same intensity as the fundamentals themselves. In general, we find that this

[11] Jones, *J. Chem. Phys.*, 1956, **25**, 1069; 1958, **28**, 1234.
[12] Tramer, *Compt. rend.*, 1959, **249**, (*a*) 2531, (*b*) 2755.
[13] Reid, *J. Chem. Phys.*, 1950, **18**, 1512.
[14] Kinell and Strandberg, *Acta Chem. Scand.*, 1959, **13**, 1607.
[15] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1958, p. 350.
[16] Chamberlain and Bailar, *J. Amer. Chem. Soc.*, 1959, **81**, 6412.

TABLE 3.

Infrared frequencies ($cm.^{-1}$) of the thiocyanate group.

Compound	Mull (M) or soln. (S)	C–N stretch (NCS anti-symmetric)	C–S stretch (NCS symmetric)	NCS bending Fundamental *	NCS bending Overtone
Isothiocyanates					
$(NH_4)_3V(NCS)_6,4H_2O$	M	2076—2078 s	830 vw	478 m	966—950 m, br
$K_3Cr(NCS)_6,4H_2O$ [a]	M	2105 s	820 vw	476 m	961 wm
	S	2092 s			
$Tl_3Cr(NCS)_6$	M	2106 s	820 w	—	—
$NH_4[Cr(NH_3)_2(NCS)_4]$	M	2120 s, 2055 sh	823 w	466 m	955 w
	S	2071 s			
py $H[Cr(NH_3)_2(NCS)_4]$	M	2085 s	836 w	—	—
Choline$[Cr(NH_3)_2(NCS)_4]$	M	2081 s	(879 w)	—	—
$K_2Co(NCS)_4,4H_2O$ [a]	M	2093—2097 s, 2065 sh	820 vw	475 m	950 wm
	S	2076 s			
$K_4Ni(NCS)_6,4H_2O$	M	2123 sh, 2101 s	766 w	469 m	940 w
	S	2072 s			
$K_2Zn(NCS)_4,4H_2O$	M	2101 sh, 2076 s	822 sh, 815 vw, 802 sh	479 w, 470 w, (412 w)	974—955 w, br
	S	2079 s			
Thiocyanates					
$K_3Rh(SCN)_6$ [a]	M	2110 sh, 2098 s, 2084 s	705 w, 695 sh	471 vw, 452 vw, 438 wm	939 vw, 893 vw, 884 w
	S	2106 s			
$Tl_3Rh(SCN)_6$	M	2088 s, 2066 s	706 w	465 w, 428 w	939 vw, 859 w, 851 sh
$K_2Pd(SCN)_4$	M	2122 s, 2116 sh, 2098 sh, 2092 sh, 2088 s, 2047 w	708 sh, 703 w, 694 sh	473 w, 465 w, 439 w, 430 w	940 vw, 927 vw, 883 vw, 873 vw, 865 vw
	S	2108 s			
$K_2Cd(SCN)_4,2H_2O$ [b]	M	2112 sh, 2093 s	754 wm, 726 wm	466 w, 458 m, 453 m, 417 w	940 vw, 929 vw, 909 vw
	S	2125 s, 2073 sh			
$K_2Pt(SCN)_6$	M	2128 sh, 2122 s, 2115 s, 2075 w	699 sh, 694 w, 686 sh	464 w, 426 w, 415 w	918 vw, 858 vw, 840 vw
	S	2120 s			
$K_2Pt(SCN)_4$	M	2127 s, 2098 s	(705 sh), 700 w, 692 sh	479 w, 472 w, 437 wm, 427 wm, 417 w	952 vw, 939 vw, 881 vw, 871 vw, 865 vw
	S	2114 s			
$K_2Hg(SCN)_4$ [a]	M	2132 s, 2119 s	716 w, 710 w, 705 w	461 m, 457 sh, 436 sh, 431 m, 416 w, br	920 w, 883 w
Molybdenum complexes					
$K_3Mo(CNS)_6,4H_2O$ [a]	M	2093 sh, 2077 s	820 w	476 wm	953 wm, br
	S	2071 s			
$K_3Mo(CNS)_6,CH_3{\cdot}CO_2H,H_2O$	M	2105 sh, 2084 s, 2048 sh	811 w	—	955 w, 943 w
	S	2062 s			
$(NH_4)_3Mo(CNS)_6,4H_2O$	M	2070 s	815 w	—	953 w, br
	S	2070 s			
$(NH_4)_3Mo(CNS)_6,HCl,H_2O$	M	2070—2075 s	813 w	474 wm, br	950 w, br
$(NH_4)_3Mo(CNS)_6,C_2H_5{\cdot}OH,H_2O$	M	2100 s	814 w	—	950 w, br
$(pyH)_3Mo(CNS)_6,3H_2O$	M	2078 sh, 2051 s	826 w, br	—	960 m, br
	S	2061 s			
$Tl_3Mo(CNS)_6$	M	2066 s	812 w	—	940 wm, br

M mull (normally in paraffin), S solution (in acetophenone).
* Normal limit 410 $cm.^{-1}$; compounds marked (*a*) examined down to 375 $cm.^{-1}$ by Dr. J. Bertie.
(*b*) $[Cd(SCN)_4]^{2-}$ contains two terminal –SCN and two bridging –SCN– groups.

applies to the isothiocyanates, but not to the thiocyanates (where the overtones appear weaker).

Table 3 shows that the C–S frequencies fall into two groups, all those for the thiocyanates lying near 700 (694—723) cm.$^{-1}$ and all those for isothiocyanate complexes higher, around 820 (760—880) cm.$^{-1}$. The " bending " frequencies also show a clear difference in trend between the two types of complex. The isothiocyanates have a band or bands of medium intensity lying near 470 cm.$^{-1}$, while the thiocyanates show, first, a shift to lower values and intensities and, secondly, a wider separation and greater number of frequencies. With the C–N frequencies, values lie higher, in general, for the thiocyanates than for the isothiocyanates but overlap occurs, as between $[Cr(NH_3)_2(NCS)_4]^-$ and $[Hg(SCN)_4]^{2-}$. To check for crystal effects we have compared C–N frequencies in acetophenone solution and these results are included in Table 3. The isothiocyanates exhibit varying behaviour: some show no change between solid and solution but others a pronounced drop in frequency, *e.g.*, $[Cr(NH_3)_2(NCS)_4]^-$ from 2120 to 2070 cm.$^{-1}$; $[Co(NCS)_4]^{2-}$ from 2095 to 2076 cm.$^{-1}$. We do not consider that dissociation affects these results. For the thiocyanates in solution the average of the two C–N frequencies shows either no change or a small increase in frequency. However, Johnson and Basolo [17] have reported for $[Pt\ en_2(SCN)_2](NO_3)_2$ a marked drop in frequency. A further feature from our results is that all thiocyanates exhibit in the solid state two main C–N bands. If the metal–thiocyanate attachment is not linear we should expect at least two bands for all complexes: for the isothiocyanates there is no clear indication of this, even with high resolution. However, in solution spectra the C–N band broadens and becomes Gaussian in shape, but no splitting is observed.

Previous investigations have been concentrated on the measurement of C–N frequencies to decide between thiocyanato- and isothiocyanato-bonding, for both organic [18] and inorganic compounds.[19] Mitchell and Williams [20] have recently examined this criterion in extensive detail for inorganic complexes and have made some broad correlations. Difficulty arises in that the C–N frequency is affected by a number of variables apart from the donor atom, and particularly in that overlap between the two classes occurs.

With C–S frequencies, however, the position does appear to be more clear-cut. There is evidence in several respects that this frequency follows structural changes more closely than does the C–N frequency. Thus where thiocyanate groups serve two functions in the structure, as in $Cd(SCN)_4^{2-}$ or $Ni(NH_3)_2(NCS)_2$,* two separate bands have been observed. Splitting effects have been noted in $[Zn(NCS)_4]^{2-}$ and $[Hg(SCN)_4]^{2-}$, as would be expected from symmetry considerations. Only one band has been noted for $[Co(NCS)_4]^{2-}$, but the difficulty here may have been connected with the low intensity of the band. The C–S frequencies also reflect the C–S bond lengths in the set of Reinecke salts {C–S = 1·80 Å in $NH_4[Cr(NH_3)_2(NCS)_4]$, 1·76 in $C_5H_6N[Cr(NH_3)_2(NCS)_4]$, 1·64 in $Me_3N{\cdot}CH_2{\cdot}CH_2{\cdot}OH[Cr(NH_3)_2(NCS_4]$; cf. C–N bond lengths of 1·14, 1·15, and 1·37 Å respectively}. In comparing C–S frequencies it is of interest that the two groups lie on either side of the value for NCS^- in KNCS, *viz.*, 749 cm.$^{-1}$. Jones has considered three possible forms for this ion, (*a*), (*b*), and (*c*), and has calculated that form (*a*) predominates (71%). With this basis the change in C–S frequency between KNCS and the complexes we have considered can be understood. *X*-Ray results imply that, for sulphur bonding, form (*g*) is important, whilst for nitrogen bonding form (*f*) or (*d*) occurs.

This would agree with the fact that where there is co-ordination to nitrogen electron drift will occur towards the nitrogen, that is, a structure of the type (*f*) should be stabilised,

* Personal communication from Dr. N. Gill, Imperial College of Science and Technology, London.

[17] Johnson and Basolo, *J. Inorg. Nuclear Chem.*, 1960, **13**, 36.

[18] Lieber, Rao, and Ramachandran, *Spectrochim. Acta*, 1959, **13**, 296; Hoyer, *Chem. Ber.*, 1956, **89**, 2677.

[19] Fujita, Nakamoto, and Kobayashi, *J. Amer. Chem. Soc.*, 1956, **78**, 3296; Rao, Ramachandran, Shankar, *J. Sci. Ind. Res., India*, 1959, **18**, *B*, 169.

[20] Mitchell and Williams, *J.*, 1960, 1912.

whilst for sulphur-co-ordination electron drift will occur towards the sulphur, which would favour structure (*g*). For the sulphur-bonded ligand we should therefore always expect a bent M–S–C bond, whilst for the nitrogen either a linear (*d*) or a bent (*f*) bond is possible for the M–N–C linkage.

Free ion	Metal–N bonding ⟷	Metal–S bonding
(*a*) $N\equiv C-S^-$	(*d*) $M-\overset{+}{N}\equiv C-S^-$	(*g*) $M\diagup S-C\equiv N$
(*b*) $^-N=C=S$	(*e*) $^-M=\overset{+}{N}=C=S$	(*h*) $M\diagup {}^+S=C=N^-$
(*c*) $^{2-}N-C\equiv S^+$	(*f*) $M\diagup N=C=S$	(*i*) $^-M=\overset{2+}{S}=C=N^-$

On the basis of the similarity of the spectra of $[Mo(CNS)_6]^{3-}$ and other isothiocyanates, particularly in regard to the C–S frequency, we suggest that bonding in these molybdenum complexes occurs to the nitrogen atom. Indirect evidence in favour of this is also given by the difference in *X*-ray powder patterns of the hexathiocyanates of rhodium on the one hand and chromium and molybdenum on the other. From optical measurements, isomorphism between $K_3Cr(CNS)_6,4H_2O$ and $K_3Mo(CNS)_6,4H_2O$ has been reported.[21] We have confirmed this by using *X*-ray methods and have determined also that isomorphism persists in the dehydrated salts. In neither case do the patterns show any correspondence with those of $K_3Rh(SCN)_6$. The same result is found when the thallium(I) salts of the three complexes are compared. Introduction of the large thallium(I) ions into the crystal lattice might be expected to minimise minor effects due to the presence of water molecules. Zhdanov *et al.*[22] have reported the cell constants for the potassium salts of the hexathiocyanates of Cr(III), Ni(II), Rh(III), and Pt(IV). It is of interest that the chromium and nickel, and hence from our result molybdenum(III) also, are closely related in spite of differences in stoicheiometry.

Additional evidence is also afforded by the ultraviolet and visible spectra of the compounds. Recently, Schäffer [4] has suggested that it is possible to differentiate between an isothiocyanate and a thiocyanate structure on the basis of the position of the ligand in the spectrochemical series. The thiocyanate group is considered to be approximately in the same position as chloride in the series, whilst the isothiocyanate falls between water and ammonia, *i.e.*, $Cl \approx {}^-SCN < F < H_2O < {}^-NCS < NH_3 < CN$. In agreement with Schäffer, we find that for $K_3Rh(SCN)_6$ a ligand-field band is observed at 20,000 cm.$^{-1}$ as compared with 19,300 cm.$^{-1}$ for the complex K_3RhCl_6. Since the first ligand-field band for $[MoCl_6]^{3-}$ has been assigned [23] at 19,000 cm.$^{-1}$, the corresponding band for the thiocyanate complex would be expected at 19,000—20,000 cm.$^{-1}$, or for an isothiocyanate at 23,000—24,000 cm.$^{-1}$. In the spectrum of $K_3[Mo(CNS)_6]$ no band was observed in the thiocyanate region (Fig. 2). However, the isothiocyanate region is masked by the presence of an electron-transfer band, which makes the determination of the presence of a ligand-field band virtually impossible. This evidence may therefore be taken as pointing indirectly to nitrogen bonding.

Molybdenum(III), thus, appears to be the first element in the second-row transition elements in which bonding occurs through the nitrogen rather than sulphur. The main study of thiocyanate bonding in this series has been restricted to elements further to the right-hand side of the transition block than molybdenum, *i.e.*, to Rh, Pd, Ag, Cd.

The question arises why some metals prefer to bond to the nitrogen and some to the

[21] Steinmetz, *Z. Krist.*, 1909, **46**, 377.
[22] Zhdanov, Zvonkova, and Glushkova, *Zhur. fiz. Khim.*, 1953, **27**, 106.
[23] Jørgensen, "Absorption Spectra of Complexes of Heavy Metals," Tech. Rept., European Res. Office U.S. Dept. Army, 1958.

sulphur of the (NCS) group. In proposing an explanation,* we make the following assumptions that: (*a*) in the $(NCS)^-$ ion the lone pairs on the sulphur atom are more easily polarised than those on the nitrogen atom; (*b*) the permanent lone-pair dipole on the nitrogen atom is larger than that on the sulphur atom; (*c*) the way in which the (NCS) group is bound (*i.e.*, through S or N) will be decided by the relative bond energies of a covalent metal–S bond and of the more ionic metal–N bond. For a covalent bond, we further assume that the bond strength is roughly proportional both to the total ionisation potential and to the overlap integral, but as a simplification we shall use total ionisation potential alone as a guide to the relative strengths of covalent bonds between different metal atoms and the same ligand. To compare the relative strengths of ionic bonds

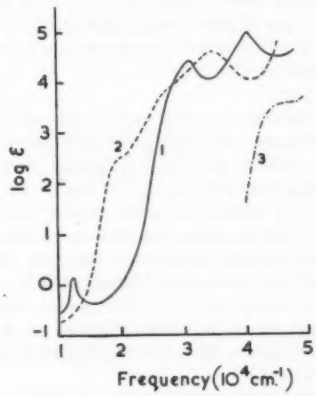


FIG. 2. Absorption spectra in aqueous solution of (1) $K_3Mo(CNS)_6.4H_2O$, (2) $K_3Rh(SCN)_6$, and (3) KNCS.

we use the expression ne/r, where r is the radius of the metal ion and ne is the formal charge on the ion. For reasons discussed elsewhere the expression $(ne)^2/r$ is sometimes more convenient. Here we shall compare only metal atoms having the same oxidation state and hence it is irrelevant whether ne or $(ne)^2$ is used. If we now compute the ratio $R =$ I.P. $\frac{ne}{r}$ (cf. Williams [24]), where I.P. is the ionisation potential in volts, and r is in Å, a number between 5 and 20 is obtained. This number is related to the ratio of the strength of a bond if covalent to its strength if ionic. We assume that the higher values of R indicate covalent binding and hence a metal–sulphur link. For univalent ions one obtains values of $R = 7$ if the metal falls into class (*b*) (*e.g.*, Cu^+, Ag^+, Au^+, Tl^+) whereas it is about 6·5 or less for those which fall into class (*a*) (*e.g.*, Li^+ or Na^+). Similarly, for bivalent ions, class (*b*) metals have R values of 10 or more, whereas those for class (*a*) metals are less than this figure (*e.g.*, Pb^{2+} 12·5, Hg^{2+} 16·0, whereas Mg^{2+} 7·4). For tervalent ions the distinction is not so obvious, the borderline between class (*a*) and class (*b*) lying about 12. Now there is considerable doubt as to the ionic radius of Mo^{3+}. Values between 0·70 and 0·78 Å have been put forward, but in either case one obtains R values *less* than the figure obtained for the undoubtedly S-bonded Rh^{3+} ion. It is not suggested that R proves that the binding is to nitrogen but rather that it provides an explanation for the borderline position of molybdenum(III) and establishes that it is more likely to form a metal–nitrogen link that is rhodium.

Finally, it is of interest that, in agreement with our conclusions, Jørgensen,[25] on the basis of the nephelauxetic series, places molybdenum(III) before chromium(III) and iron(III),

* This proposal refers only to those complexes in which all ligands are $[SCN]^-$.

[24] Williams, *Proc. Chem. Soc.*, 1960, 20.
[25] Jørgensen, *Acta Chem. Scand.*, 1958, **12**, 903.

i.e., he suggests that it has a greater tendency to form bonds with considerable ionic character and hence to favour N- over S-bonding in thiocyanate complexes.

Experimental

Preparations.—*Tripotassium hexathiocyanatomolybdate*(III),$4H_2O$. This was prepared as described by Maas and Sand [26] [Found: K, 18·6; Mo, 15·0, 15·1; C, 11·5; N, 12·6; S, 30·0; H, 1·5. Calc. for $K_3Mo(CNS)_6,4H_2O$ (for $5H_2O$ in parentheses): K, 18·5 (18·0); Mo, 15·1 (14·7); C, 11·4 (11·1); N, 13·3 (12·9); S, 30·35 (29·5); H, 1·3 (1·5)%].

Tripotassium hexathiocyanatomolybdate(III),AcOH,H_2O. Dilute acetic acid was added in excess to a moderately concentrated aqueous solution of the tetrahydrate.[26] Amber-coloured crystals were deposited on cooling and storage [Found: Mo, 15·6; C, 15·3; N, 14·0; H, 1·6. Calc. for $K_3Mo(CNS)_6,CH_3{\cdot}CO_2H,H_2O$: Mo, 15·0; C, 15·0; N, 13·1; H, 1·0%].

Triammonium hexathiocyanatomolybdate(III),$4H_2O$ was prepared as detailed by Palmer [27] [Found: C, 12·9; N, 22·5; H, 3·5. Calc. for $(NH_4)_3Mo(CNS)_6,4H_2O$: C, 12·6; N, 22·1; H, 3·5%].

Triammonium hexathiocyanatomolybdate(III),$C_2H_5{\cdot}OH,H_2O$. The tetrahydrate was dissolved in ethanol and the solution filtered. Addition of benzene precipitated the compound as a fine yellow powder [27] (Found: Mo, 16·9; C, 15·9; N, 20·4; S, 34·8; H, 3·6. Calc. for $(NH_4)_3Mo(CNS)_6,C_2H_5{\cdot}OH,H_2O$: Mo, 17·05; C, 17·1; N, 22·4; S, 34·2; H, 3·6%). In the infrared spectrum bands arising from ethanol were observed at 1250w, 1027m, 866w cm.$^{-1}$.

Triammonium hexathiocyanatomolybdate(III),HCl,H_2O was obtained on cooling a concentrated hydrochloric acid solution of the tetrahydrate.[27] The yellow crystals were not as stable on storage as the alcoholate.

Trithallium(I) *hexathiocyanatomolybdate*(III),xH_2O. Thallous acetate or nitrate solution, added to an aqueous solution of $K_3Mo(CNS)_6,4H_2O$, produced an immediate orange-yellow precipitate. This was washed with water and dried over P_2O_5. On storage in air the compound darkened.[28]

Tripyridinium hexathiocyanatomolybdate(III),$3H_2O$ was prepared by the addition of pyridine to an aqueous solution of $K_3Mo(CNS)_6$ acidified with acetic acid [29] [Found: Mo, 13·3; N, 17·3. Calc. for $(C_5H_5N)_3Mo(CNS)_6,3H_2O$: Mo, 13·0; N, 17·1%].

Tetrapotassium heptacyanomolybdate(III),$2H_2O$ was prepared from K_3MoCl_6 [6] and similarly from K_2MoCl_5,H_2O. The compound separated as fine dark crystals, with a green tinge and dull lustre [Found: K, 34·2; Mo, 20·5; C, 18·3; N, 20·4; H, 1·0. Calc. for $K_4Mo(CN)_7,2H_2O$: K, 33·2; Mo, 20·4; C, 17·9; N, 20·8; H, 0·9%].

Trithallium(I) hexathiocyanatochromate(III),xH_2O was precipitated as a greyish-pink powder on addition of a thallous salt to a solution of $K_3Cr(NCS)_6$.

Tripotassium hexathiocyanatorhodate(III) was prepared by Barbieri's method [30] except that K_2RhCl_5 was used as starting material {Found: K, 21·5 (by direct precipitation with $[BPh_4]^-$); C, 12·2; N, 15·9. Calc. for $K_3Rh(SCN)_6$: K, 20·5; C, 12·7; N, 14·8%}.

Trithallium(I) *hexathiocyanatorhodate*(III). Addition of a solution of thallous acetate to an aqueous solution of the above potassium salt produced immediately an orange-red precipitate. This was filtered off and washed with water. It was stable on storage.

Dipotassium hexathiocyanatoplatinate(IV),$2H_2O$ was obtained by long digestion of potassium chloroplatinate(IV) with the stoicheiometric amount of potassium thiocyanate followed by extraction with alcohol [31] [Found: K, 11·9; C, 12·1; N, 13·3; H, 0·4. Calc. for $K_2Pt(CNS)_6$: K, 11·9; C, 10·95; N, 12·8; H, 0·6%]. This material and another sample prepared by Dr. M. Baldwin gave an identical infrared spectrum.

Dehydration.—(i) $K_3Mo(CNS)_6,4H_2O$: Weight loss on vacuum-treatment was assessed by plotting loss against time (dehydration was accompanied by a small amount of decomposition even in the absence of oxygen). The loss so found corresponded to removal of four mol. of water (11·4%. Calc. for $4H_2O$: 11·4%). The buff-coloured dehydrated compound gave an

[26] Maas and Sand, *Ber.*, 1908, **41**, 1506.
[27] Palmer, " Experimental Inorganic Chemistry," Cambridge Univ. Press, 1954.
[28] Rosenheim and Garfunkel, *Ber.*, 1908, **41**, 2388.
[29] Barbieri, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1930, **12**, 55.
[30] Barbieri, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1931, **13**, 434.
[31] Buckton, *J. prakt. Chem.*, 1855, **64**, 65.

infrared spectrum similar to that of the tetrahydrate but lacking OH and H–O–H peaks. With another preparation a direct determination of the loss gave a value of 12·15% (without correction as above), but the product on storage over sodium carbonate decahydrate [27] showed an increase in weight corresponding to 11·45% of the original sample.

The splitting observed in the H–O–H frequencies in the infrared spectrum suggested the possibility of a non-equivalence of water molecules in the structure. Deuteration, performed by dehydrating the material as above and then exposing it to D_2O vapour, resulted, however, in an exactly similar pattern with the expected shift in frequencies (see Table 4).

(ii) $(NH_4)_3Mo(CNS)_6,4H_2O$. Dehydration over sulphuric acid or *in vacuo* did not produce a water-free product. The material so obtained when stored over sodium carbonate decahydrate increased in weight by 10·0%, corresponding with an uptake of 3 mol. of water. (Calc.: 10·5%). The infrared spectrum of the compound again displayed a splitting of the ν_2 water band but with some shift of frequency.

TABLE 4.

Infrared frequencies observed for the ν_2H_2O band ($cm.^{-1}$).

$K_3Mo(CNS)_6,4H_2O$	1653—1655 sh,	1626—1628 wm
$K_3Mo(CNS)_6,4D_2O$	~1640 w,	1208 sh, 1170 wm
$(NH_4)_3Mo(CNS)_6,4H_2O$	1621—1626 sh,	1608—1610 wm
$(NH_4)_3Mo(CNS)_6,HCl,H_2O$	~1621 w	
$(NH_4)_3Mo(CNS)_6,EtOH,H_2O$	1637—1639 w	

(iii) $(NH_4)_3Mo(CNS)_6,C_2H_5{\cdot}OH,H_2O$. Vacuum-treatment resulted in loss of alcohol and retention of water [Found: loss, 7·9. Calc. for $(NH_4)_3Mo(CNS)_6,H_2O$: H_2O, 8·2%]. This result was confirmed by changes in the infrared spectrum.

(iv) $(NH_4)_3Mo(CNS)_6,HCl,H_2O$. The end-product on vacuum-treatment showed retention of water [Found: Mo, 18·6; S, 37·4. Calc. for $(NH_4)_3Mo(CNS)_6,H_2O$: Mo, 18·6; S, 37·2. Calc. for $(NH_4)_3Mo(CNS)_6,HCl$: Mo, 17·9; S, 34·8%].

Spectra.—Infrared spectra were obtained by using paraffin or hexachlorobutadiene mulls with sodium chloride or polystyrene-coated potassium bromide plates as necessary. Acetophenone was used as a solvent for the solution measurements. Evaporation of an acetone solution on a preheated plate was employed to produce a thin crystal film where desirable, to confirm other results. The spectrometer was a Grubb–Parsons grating instrument of type GS2A. Determinations of bending frequencies (in the 500—375 $cm.^{-1}$ region) were supplemented by measurements on a Unicam S.P. 100 spectrometer fitted with a potassium bromide prism.

Ultraviolet and visible spectra were determined with a Unicam S.P. 500 or Carey model 10 spectrophotometer. Magnetic-susceptibility measurements were carried out on the apparatus described earlier [22] and in calculations of magnetic moments the usual diamagnetic corrections were made.

We are indebted to Dr. N. Gill for a number of thiocyanate complexes and for discussions, and also to Dr. F. E. Mabbs for measurements of the temperature-dependence of susceptibility and for the vanadium(III) compound. One of us (P. W. S.) gratefully acknowledges a Du Pont studentship.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORY,
UNIVERSITY COLLEGE, GOWER STREET,
LONDON, W.C.1.

[*Received, March 17th,* 1961.]

[22] Figgis and Nyholm, *J.*, 1959, 331.

XUM

900. *Ferrocene Derivatives. Part VIII.* Tetrahydropyridoferrocenes.*

By J. M. Osgerby and P. L. Pauson.

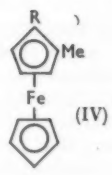
The rearrangement product of (ferrocenylmethyl) trimethylammonium iodide (I) is shown to be dimethyl 2-(ferrocenyl)ethylamine (III). The corresponding primary amine (VIII; R = H) is converted by various routes into di- and tetra-hydropyridoferrocenes.

The preparation of (ferrocenylmethyl)trimethylammonium iodide (I) was first described by Hauser *et al.*[1] who also studied its rearrangement under the influence of amide ions. This reagent must cause initial hydrogen abstraction, yielding an equilibrium mixture of the zwitterions (IIa) and (IIb), in which the former may be presumed to predominate. These can then undergo a Stevens rearrangement to (IIIa or b), respectively; alternatively the zwitterion (IIb) could rearrange by a cyclic mechanism to the amine (IV; R = $CH_2{\cdot}NMe_2$). The last possibility, while analogous to the "*ortho*-rearrangement" of benzyltrimethylammonium salts, involves a much less favourable transition state for the ferrocene case, where there are two fused five-membered rings.[2] Hauser and his co-workers[3] rejected this, their original formulation (IV; R = $CH_2{\cdot}NMe_2$) for the product,

$Fc{\cdot}CH_2{\cdot}NMe_3^+\ I^-$ (Fc = ferrocenyl)
(I)

$Fc{\cdot}\bar{C}H{\cdot}NMe_3^+$ (a) ⟷ $Fc{\cdot}CH_2{\cdot}\overset{+}{N}Me_2{\cdot}CH_2^-$ (b)
(II)

$Fc{\cdot}CHMe{\cdot}NMe_2$ (a) ⟷ $Fc{\cdot}CH_2{\cdot}CH_2{\cdot}NMe_2$ (b)
(III)



(IV)

when they observed its Hofmann degradation to vinylferrocene. This evidence is consistent with either structure (IIIa or b), but they were able to eliminate the former by an independent synthesis. That (IIIb) is the structure of the rearrangement product confirms the expectation that the ferrocenylmethyl group, like the benzyl group, would migrate much more readily than methyl, this difference outweighing the effect of the probable position of equilibrium (IIa ⟷ b).

$Fc{\cdot}CH_2{\cdot}CN$ (V) $Fc{\cdot}CH(CN){\cdot}NMe_2$ (VI) $Fc{\cdot}CH_2{\cdot}CS{\cdot}NMe_2$ (VII) $Fc{\cdot}CH_2{\cdot}CH_2{\cdot}NHR$ (VIII)

However, in deducing structure (IIIb), Hauser *et al.*[3] assigned structure (IV; R = CN) to the product obtained by the action of cyanide ions on the quaternary salt (I). Having proved that this nitrile has the unrearranged structure (V),[4] we reinvestigated the evidence. An alternative synthesis of the tertiary amine (IIIb) appeared desirable, since its structure had been arrived at by a process of elimination. Moreover, its isomer (IIIa) had been synthesised[5] by the reaction of the amino-nitrile (VI) with methylmagnesium iodide, a method which is established in analogous systems[6] but is nevertheless somewhat ambiguous.

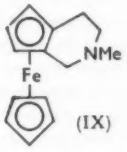
Acetylferrocene with sulphur and dimethylamine gave the thioamide (VII), which was reduced in crude form to the amine (IIIb), identical with the rearrangement product. A third method of obtaining this amine, albeit only in the form of its methiodide, was

* Part VII, Knox and Pauson, *J.*, 1958, 692.

[1] Hauser and Lindsay, *J. Org. Chem.*, 1956, **21**, 382.
[2] Cf. Osgerby and Pauson, *Chem. and Ind.*, 1958, 196.
[3] Hauser, Lindsay, Lednicer, and Cain, *J. Org. Chem.*, 1957, **22**, 717.
[4] Part VI, Osgerby and Pauson, *J.*, 1958, 656.
[5] Hauser and Lindsay, *J. Org. Chem.*, 1957, **22**, 906.
[6] Stevens *et al.*, *J.*, 1931, 2568; 1932, 2607.

reduction of the cyanide (V) to the primary amine (VIII; R = H) followed by methylation with methyl iodide. The identity of the quaternary salt obtained with that of the rearrangement product was established by comparison of melting points, infrared spectra, and *X*-ray powder diagrams. In the methylation step we avoided the use of formaldehyde–formic acid (the reagent commonly preferred for analogous reactions since it yields the free tertiary amine), realising [2] that it might lead to cyclic products such as (IX). It proved indeed to be this cyclisation which had misled Hauser *et al.*[7] Although at one time they had rejected [7] a cyclic formulation for the formaldehyde–formic acid reaction product, they have recently [8] obtained degradative evidence which supplements and confirms our own synthetic evidence [9] for structure (IX), obtained as follows.

The formation of the cyclic (IX) from the " open " base (VIII; R = H or Me) involves cyclisation of an intermediate of type (X; R = H or Me). It may thus be regarded as an internal aminomethylation analogous to that used to prepare the starting material (I). We therefore first carried out such a process stepwise. Reaction of the primary amine (VIII; R = H) with alkyl sulphates was found to stop at the secondary amine stage. Formaldehyde converted the *N*-methyl derivative (VIII; R = Me) into the methylenebis-derivative (XI) which was then cyclised to the tetrahydropyridoferrocene (IX) identical with a sample obtained [7] from the primary amine (VIII; R = H) in one step with formaldehyde and formic acid.



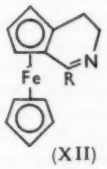
(IX)

$Fc{\cdot}CH_2{\cdot}CH_2{\cdot}NR{\cdot}CH_2^+$

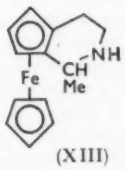
(X)

$(Fc{\cdot}CH_2{\cdot}CH_2{\cdot}NMe)_2CH_2$

(XI)



(XII)



(XIII)

Alternatively under Bischler–Napieralski conditions *N*-formyl-2-(ferrocenyl)ethylamine (VIII; R = CHO) gave the dihydropyridoferrocene (XII; R = H) which was reduced and methylated to yield the amine (IX), whose methiodide was identical with methiodides of each of the two samples mentioned above.

In the same way the *N*-acetyl derivative (VIII; R = Ac) of the primary amine yielded 1′,2′,5′,6′-tetrahydro-1′-methylpyrido(3′,4′)ferrocene (XIII). Since the methyl group in this compound can be on the same side of the fused ring system as the iron atom, or on the opposite side, two geometrical isomers (each a racemic pair) are possible. However, no separation occurred on chromatography of the product, which yielded a crystalline picrate. Thus a single isomer appears to be obtained under these conditions and an attempt to obtain the second stereoisomer by catalytic hydrogenation (Adams catalyst) (in place of reduction by lithium aluminium hydride) of the intermediate 5′,6′-dihydro-2′-methylpyrido(3′,4′)ferrocene (XII; R = Me) failed. We also failed to dehydrogenate this dihydroisoquinoline analogue (XII; R = Me) with a variety of reagents.

Experimental

2-(Ferrocenyl)ethylamine (VIII; R = H).—A solution of ferrocenylacetonitrile [4] (16·5 g., 0·073 mole) in ether was added dropwise during 30 min. to lithium aluminium hydride (6·3 g., 0·17 mole) in ether. The mixture was stirred at room temperature overnight. The excess of hydride was destroyed by addition of moist ether (use of ethyl acetate led to the formation of the *N*-acetyl derivative as a major by-product along with the amine). After later addition of water, the mixture was filtered, the organic layer separated, dried, and evaporated, and the

[7] Lednicer, Lindsay, and Hauser, *J. Org. Chem.*, 1958, **23**, 653.
[8] Lednicer and Hauser, *J. Org. Chem.*, 1959, **24**, 43.
[9] Osgerby and Pauson, *Chem. and Ind.*, 1958, 1144.

residual oil distilled at 120—125°/0·5 mm., giving 2-(ferrocenyl)ethylamine (13·5 g., 83%) (Found: C, 62·2; H, 6·2; N, 6·1. Calc. for $C_{12}H_{15}FeN$: C, 62·9; H, 6·6; N, 6·1%).

N-*Acetyl*-2-(*ferrocenyl*)*ethylamine* (VIII; R = Ac).—Acetic anhydride (5 ml.) was added to the amine (VIII; R = H) (5·9 g.) in benzene (30 ml.) and the mixture refluxed for ½ hr. under nitrogen, then poured into water. The benzene layer was separated, dried, and evaporated, and the residue recrystallised from cyclohexane. The *acetyl derivative* formed yellow plates, m. p. 117—118° (4·5 g., 65%) (Found: C, 61·9; H, 6·2; N, 4·8. $C_{14}H_{17}FeNO$ requires C, 62·0; H, 6·3; N, 5·2%).

N-*Formyl*-2-(*ferrocenyl*)*ethylamine* (VIII; R = CHO).—To a solution of the amine (VIII; R = H) (11·45 g., 0·05 mole) in ether (200 ml.) was added dropwise a solution of n-butyl-lithium, prepared from lithium (1 g.) and n-butyl bromide (8·56 g.) in ether. After 1 hour's stirring under nitrogen, ethyl formate (5 g., 0·07 mole) in ether (20 ml.) was added and stirring continued overnight. Water was then added and the ether layer separated, dried, and evaporated, yielding the *formyl derivative* (11·1 g., 86%), which crystallised from cyclohexane as yellow plates, m. p. 69—70° (Found: C, 60·7; H, 5·6; N, 5·7. $C_{13}H_{15}FeNO$ requires C, 60·7; H, 5·9; N, 5·5%).

2-(*Ferrocenyl*)*ethyldimethylamine* (IIIb).—(*a*) From the quaternary salt (I) this amine was obtained in 32% yield by following the method of Hauser *et al.*[1,10] It was characterised by its methiodide, m. p. 237° (decomp.) [Hauser *et al.* give figures varying from 240° [7] to 250° (decomp.) [10]], and picrate, m. p. 180—183° (decomp.), greenish-yellow crystals from aqueous ethanol (Hauser *et al.*[10] record m. p. 179—180°).

(*b*) Sulphur (0·67 g.), dimethylamine (25 g.), acetylferrocene (1·86 g.), and dioxan (10 ml.) were heated together in a sealed tube at 130° for 2½ hr. The mixture was evaporated to dryness under reduced pressure and extracted with dioxan. Raney nickel (*ca.* 2 g. suspended in ethanol) was added and the whole heated for 1 hr. on a steam bath. The catalyst was removed and was washed with ethanol and water, and the combined filtrate and washings were concentrated *in vacuo*. The residue was taken up in ether and extracted with dilute hydrochloric acid and the base, liberated by neutralisation of the aqueous layer, was re-extracted into ether. After drying (Na_2SO_4) and evaporation, the amine was isolated as its picrate, identical in m. p. and mixed m. p. with the sample described under (*a*). The m. p.s and infrared spectra of the methiodides were likewise identical.

(*c*) A mixture of the amine (VIII; R = H) (0·44 g.), methyl iodide (3·3 ml.), sodium hydrogen carbonate (0·5 g.), and methanol (20 ml.) was refluxed for 60 hr. Water was then added, the solution extracted with chloroform, and the organic layer separated, dried, and evaporated, leaving 2-(ferrocenyl)ethyltrimethylammonium iodide (0·30 g., 40%), m. p. 237°, undepressed on admixture with the methiodide described under (*a*). Identity of these two specimens was confirmed by comparison of infrared spectra and *X*-ray powder diagrams.

The same quaternary salt was obtained (in 61% yield) when the secondary amine (VIII; R = Me) was treated in identical fashion.

2-(*Ferrocenyl*)*ethylmethylamine* (VIII; R = Me).—Sodium (10·3 g., 0·45 g.-atom) was carefully added to a solution of 2-(ferrocenyl)ethylamine (VIII; R = H) (10 g., 0·044 mole) in methanol (300 ml.), followed dropwise by dimethyl sulphate (14 ml., 0·15 mole). The mixture was then refluxed for 4 hr. Solvent was removed *in vacuo*, water added, and the product extracted with benzene. After drying (Na_2SO_4) and evaporation of the extract, the dark oily product was chromatographed in benzene on alumina.

2-(*Ferrocenyl*)*ethylmethylamine* (7·03 g., 66%) was obtained as a brown oil, b. p. 96—98°/0·01 mm. (Found: N, 5·7. $C_{13}H_{17}FeN$ requires N, 5·8%). Its *picrate* formed brown plates (from ethanol), m. p. 182—183° (Found: C, 48·1; H, 4·1; N, 11·6. $C_{19}H_{20}FeN_4O_7$ requires C, 48·3; H, 4·3; N, 11·9%).

NN'-Methylene bis-[2-(*ferrocenyl*)*ethylmethylamine*] (XI).—2-(Ferrocenyl)ethylmethylamine (VIII; R = Me) (6·5 g., 0·027 mole) was dissolved in ethanol (200 ml.), and 30% aqueous formaldehyde (2·5 ml., 0·025 mole) was added. After refluxing for 18 hr., the solvent was removed under reduced pressure, water was added to the residue, and the mixture extracted with benzene. Evaporation of the dried benzene solution left the product (XI), a yellow-brown oil (7·0 g.), characterised as its *picrate*, m. p. 181°, which formed orange rods from aqueous ethanol (Found: C, 49·1; H, 4·3; N, 11·5. $C_{39}H_{40}FeN_8O_{14}$ requires C, 49·0; H, 4·2; N, 11·7%).

3',4'-*Dihydropyrido*(3',4')*ferrocene* (XII; R = H).—To *N*-formyl-2-(ferrocenyl)ethylamine

[10] Hauser, Lindsay, and Lednicer, *J. Org. Chem.*, 1958, **23**, 358.

(VIII; R = CHO) (5·3 g.) in benzene (50 ml.), phosphorus oxychloride (10 ml.) was added. The mixture was refluxed for 1 hr., then poured on ice, the organic layer removed, and the aqueous layer made alkaline with 2N-sodium hydroxide and extracted with benzene. This extract was dried and concentrated and the product purified by chromatography on alumina with ether as eluent. After removal of the ether *3',4'-dihydropyrido(3',4')ferrocene* (XII; R = H) (1·17 g., 50%) distilled at 125—130°/0·03 mm. as a red-brown oil (Found: C, 64·7; H, 5·6; N, 5·9. $C_{13}H_{13}FeN$ requires C, 65·3; H, 5·5; N, 5·9%).

Tetrahydro-N-methylpyrido(3',4')ferrocene (IX).—(a) *From 2-(ferrocenyl)ethylamine* (VIII; R = H).[7] 40% Aqueous formaldehyde (3·4 mol.) was carefully added to a solution of the amine (3·45 g.) in 95% formic acid (0·7 ml.). After the initial reaction had subsided the mixture was heated on a steam bath for 3 hr. The cooled solution was then poured into water, made alkaline with 2N-sodium hydroxide, and extracted with ether. Evaporation, and distillation at 123—125°/0·7 mm., gave the tetrahydro-*N*-methylpyridoferrocene (IX) (2·7 g., 70%) (Found: C, 65·9; H, 6·8; N, 5·4. Calc. for $C_{14}H_{17}FeN$: C, 65·9; H, 6·7; N, 5·5%), characterised by its methiodide,[3,7] m. p. 258° (decomp.) (from $CHCl_3$), and picrate, orange-yellow plates (from aqueous ethanol), m. p. 161° (Found: C, 49·5; H, 4·2; N, 11·1. Calc. for $C_{20}H_{20}FeN_4O_7$: C, 49·6; H, 4·2; N, 11·6%).

(b) *From methylenebis-*[2-*(ferrocenyl)ethylmethylamine*] (XI). A solution of this precursor (XI) (7 g.) and phosphoric acid (2 drops; *d* 1·75) in glacial acetic acid (50 ml.) was heated on a water bath for 18 hr., then poured into water and neutralised with 2N-sodium hydroxide. Extraction with ether and removal of the solvent left a dark oil (4·7 g.) which was chromatographed in benzene on alumina. The second of four bands formed yielded tetrahydro-*N*-methylpyrido(3',4')ferrocene (IX) (0·6 g., 17%), whose methiodide was indistinguishable in m. p., mixed m. p., and infrared spectrum from the sample described under (a) above.

(c) *From 3',4'-dihydropyrido(3',4')ferrocene* (XII; R = H). A solution of this unsaturated cyclic base (0·47 g.) in anisole was added to an excess of lithium aluminium hydride in anisole. The mixture was stirred at room temperature under nitrogen for 3 hr. and the excess of hydride then destroyed by moist ether followed by water. The product was extracted from the organic phase with 2N-hydrochloric acid, liberated with 2N-sodium hydroxide, and then re-extracted into benzene. Removal of this solvent left the tetrahydropyridoferrocene (0·24 g.) which was not purified but was dissolved in methanol containing sodium methoxide and treated with an excess of dimethyl sulphate. The mixture was refluxed for 1 hr., cooled, and treated with water. Extraction of the resultant tetrahydro-*N*-methylpyridoferrocene with ether followed by addition of methyl iodide to the ether solution precipitated the methiodide, identical in m. p., mixed m. p., and infrared spectrum with the samples described under (a) and (b).

3',4'-Dihydro-1'-methylpyrido(3',4')ferrocene (XII; R = Me).—To *N*-acetyl-2-(ferrocenyl)-ethylamine (VIII; R = Ac) (3·9 g., 0·014 mole) in dry benzene (60 ml.), phosphorus oxychloride (20 ml.) was added, and the mixture then refluxed. After a few minutes a deep-purple colour was observed. After 1 hr. the solution was poured into water and the colourless benzene solution separated from the purple aqueous layer. Neutralisation of the latter with 2N-potassium hydroxide discharged this colour and liberated the yellow product, which was extracted into benzene. Removal of the solvent under reduced pressure left a yellow-brown oil (3·1 g., 85%), b. p. 115—120°/0·05 mm., which was chromatographed on alumina and redistilled. The *3',4'-dihydro-1'-methylpyrido(3',4')ferrocene* (XII; R = Me) so obtained solidified but could not be recrystallised (Found: C, 66·3; H, 6·0; N, 5·5, 5·6. $C_{14}H_{15}FeN$ requires C, 66·4; H, 5·9; N, 5·5%). It formed a *picrate* which, crystallised from acetone, had m. p. 214° (decomp.) (Found: C, 49·6; H, 4·2; N, 11·8. $C_{20}H_{18}FeN_4O_7$ requires C, 49·8; H, 3·8; N, 11·6%), and a *methiodide*, m. p. 203—204° (decomp.) (Found: C, 45·9; H, 5·0; N, 3·8. $C_{15}H_{18}FeIN$ requires C, 45·6; H, 4·6; N, 3·55%).

1',2',5',6'-Tetrahydro-1'-methylpyrido(3',4')ferrocene.—3',4'-Dihydro-1'-methylpyrido-(3',4')ferrocene (XII; R = Me) (1 g.) in ether was added to an excess of ethereal lithium aluminium hydride, and the mixture stirred at room temperature for 2 hr. Wet ether was then added, followed by water. The organic layer was separated, dried, and evaporated, leaving a yellow oil (0·85 g., 84%). This was chromatographed in benzene on alumina. Ether slowly eluted a single yellow band. Addition of picric acid to the eluate afforded the *tetrahydromethylpyrido(3',4')ferrocene picrate*, which crystallised from aqueous acetone as yellow plates, m. p. 196° (decomp.) (Found: C, 49·4; H, 4·35; N, 11·4. $C_{20}H_{20}FeN_4O_7$ requires C, 49·6; H, 4·2; N, 11·6%).

The authors are grateful to the Minnesota Mining and Manufacturing Company for generous financial support, and to E.I. du Pont de Nemours and Co. for gifts of ferrocene.

THE UNIVERSITY, SHEFFIELD, 10.
[Present address (P. L. P.): THE ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY, GLASGOW.] [*Received, April 10th*, 1961.]

---

901. *Ferrocene Derivatives. Part IX.* Some Disubstituted Derivatives.*

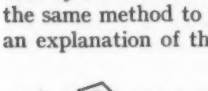
By J. M. OSGERBY and P. L. PAUSON.

Novel preparations of dimethyl ferrocene-1,1′-dicarboxylate, 1,1′-bis-(dimethylaminomethyl)ferrocene, ferrocene-1,1′-dicarboxyaldehyde, and 1,1′-dicyanoferrocene are described. Some reactions of ferrocene-mono- and -dicarboxyaldehyde are reported.

THE synthesis of substituted ferrocenes directly from the corresponding cyclopentadiene derivatives rather than by substitution of the parent compound is hampered by the inaccessibility of most such derivatives. It has therefore been limited to a few alkyl and aryl derivatives.[1]

The work described in this and the following papers was based on the consideration that substituted cyclopentadienide ions were frequently more accessible than the corresponding free cyclopentadienes and should be capable of reacting directly with ferrous chloride or other transition-metal salts. This principle has already been utilized by Benson and Lindsey [2] in their elegant synthesis of dihydroxyferrocenes.

Thiele [3] described the condensation of cyclopentadiene with diethyl oxalate, ethyl nitrite, and ethyl nitrate in presence of an excess of alkali, obtaining the sodium salts of ethoxalyl-, nitroso-, and nitro-cyclopentadiene respectively. In each case the free cyclopentadiene is unobtainable, since its liberation with acid is followed by rapid dimerisation. The salts contain the resonance-stabilised cyclopentadienide ion and are stable as monomers. Unfortunately we have not so far been able to convert any of these salts into the corresponding ferrocenes. However, when cyclopentadienylsodium was treated with methyl chloroformate in presence of excess of sodium so as to produce the sodium salt (I) of methyl cyclopentadienecarboxylate, and then with ferrous chloride, dimethyl ferrocene-1,1′-dicarboxylate was produced in 30% yield. Though illustrating the validity of the method in principle, this offers no advantage over the preparation of ferrocenedicarboxylic acid by the method of Nesmeyanov *et al.*[4] While our work was in progress Peters [5] used the same method to prepare the salt (I) and his isolation of a dicarboxylic ester provides an explanation of the low yields observed. No tri- or tetra-carboxylate of ferrocene was found in our work, whence it seems that, in common with Thiele's salts, Peters's dimethyl sodiocyclopentadienedicarboxylate is too inert towards ferrous chloride. There has also appeared a patent [6] in which the same approach is used to prepare diacetylferrocene from cyclopentadienylsodium and acetyl chloride: no detail or yield is given here: we obtained only a 2% yield of diacetylferrocene under the same conditions as used for the diester.

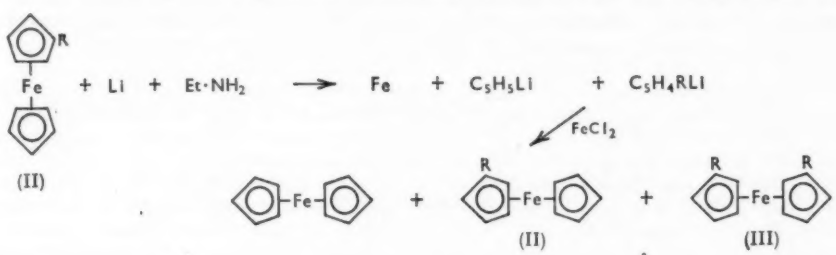


(I)

* Part VIII, preceding paper.

[1] Pauson, *J. Amer. Chem. Soc.*, 1954, **76**, 2187; Reynolds and Wilkinson, *J. Inorg. Nuclear Chem.*, 1959, **9**, 3; Riemschneider and Nehring, *Monatsh.*, 1959, **90**, 568.
[2] Benson and Lindsay, *J. Amer. Chem. Soc.*, 1957, **79**, 5471.
[3] Thiele, *Ber.*, 1900, **23**, 666; 1901, **24**, 68.
[4] Nesmeyanov, Perevalova, and Beinoravichute, *Doklady Akad. Nauk S.S.S.R.*, 1957, **112**, 439.
[5] Peters, *J.*, 1959, 1757.
[6] Lynch and Brantley, B.P. 785,760.

Another source of substituted cyclopentadiene salts is the substituted ferrocenes. Trifan and Nicholas [7] showed that ferrocene is rather smoothly degraded by lithium and ethylamine. The isolation of free cyclopentadiene on hydrolysis of the reaction mixture indicates that the cleavage leads initially to cyclopentadienyl-lithium. If the same reaction is applied to a monosubstituted ferrocene (II) a mixture of cyclopentadienyl-lithium and a substituted cyclopentadienyl-lithium results. Addition of ferrous chloride should convert this into a mixture of starting material, disubstituted ferrocene, and ferrocene. If the first step is complete and if the second takes the statistical course, then 50% of starting material (II) would be recovered and 25% of the disubstituted product (III) should result. We studied dimethylaminomethylferrocene (II; R = $CH_2 \cdot NMe_2$) since it may be made quantitatively by direct aminomethylation [8] of ferrocene, whereas the corresponding disubstitution product (III) cannot be obtained at all in this way. It was found that a rather large excess of lithium was required to effect even 80% completion of the first stage [as ascertained by decomposition of the reaction mixture with water and isolation of unchanged (II)], but addition of ferrous chloride then afforded the three products in very nearly the statistical ratio. The optimum yield of the diamine (III; R = $CH_2 \cdot NMe_2$) was ~15% (based on total iron present). It was also found that free dimethylaminomethylcyclopentadiene could not be isolated from the initial reaction mixture, which emphasised the value of direct treatment with ferrous chloride. Cyanoferrocene and methylthioferrocene failed to yield products other than ferrocene itself in a similar reaction: in both cases it appears reasonable to assume that the substituted cyclopentadienyl-lithium does not survive under the vigorous reducing conditions. The diamine (III; R = $CH_2 \cdot NMe_2$) was characterised as its picrate and dimethiodide, and the structure of the latter was demonstrated by the close similarity of its infrared spectrum to that of ferrocenylmethyltrimethylammonium iodide (II; R = $CH_2 \cdot NMe_3^+I^-$), as well



as by hydrolysis to the known diol (III; R = $CH_2 \cdot OH$). Other reactions of the bisquaternary salt are under investigation. The diol (III; R = $CH_2 \cdot OH$) is better obtained by the Russian method.[4] Using manganese dioxide,[9] we oxidised it to the dialdehyde (III; R = CHO), a stable red solid, in 33% yield. The intermediate hydroxyaldehyde was obtained as a by-product.

The dialdehyde was characterised as dioxime which was dehydrated in excellent yield to the dinitrile (III; R = CN). Nesmeyanov and Reutov [10] recently obtained the same dinitrile from ferrocenedicarboxylic acid through the diamide. The infrared spectra of these disubstituted ferrocenes (III; R = $CH_2 \cdot NMe_3I$, CHO, CN) are listed in Table 1 with those of their monosubstituted analogues for comparison.

An attempt has been made to produce derivatives in which the two rings are bridged by condensing the dialdehyde with acetone and with *o*-phenylenediamine.

The product obtained from *o*-phenylenediamine proved difficult to purify completely

[7] Trifan and Nicholas, *J. Amer. Chem. Soc.*, 1957, **79**, 2746.
[8] Osgerby and Pauson, *J.*, 1958, 656.
[9] Hauser, Lindsay, Lednicer, and Cain, *J. Org. Chem.*, 1957, **22**, 717.
[10] Nesmeyanov and Reutov, *Doklady Akad. Nauk S.S.S.R.*, 1958, **120**, 1267.

and its low solubility and poor stability in solution prevented us from determining its molecular weight. Its analysis is in approximate agreement with the bridged structure (IV).

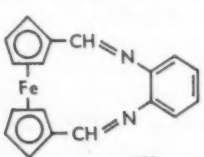
TABLE 1.

Infrared spectra of mono- and di-substituted ferrocenes (cm.$^{-1}$) (as KBr discs).

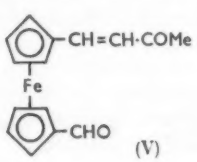
CHO		CN		$CH_2 \cdot NMe_3^+I^-$	
Mono	Di	Mono	Di	Mono	Di
1671s *	1696s	2242s	2240s	1483s	1483s
1381s	1452s			1469s	1469s
		1442m	1438m	1445s	1455s
1414m	1408m			1407m	1397m
1388m	1384m	1388m	1389m	1380m	1377m
1371s	1365s	1373m	1375m		
1332m	1332m				
1247s	1240s	1233s	1227s		
1203m	1209m			1131m	1129m
1106s		1109s		1104s	
1033s	1037s	1052s	1048s	1044m	1040m
1026s	1023s	1032s	1030s	1037m	1021m
1004s		1006s		1005s	
		912s	908s	990s	987s
		859m	861m	974s	971s
826s	830s	825s	829s	914s	924s
745s	746s			880s	877s
				851m	853m

* Doublet.

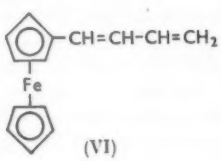
Acetone led to a product giving a positive iodoform test, whose analysis and dark colour suggested formulation as (V), but its infrared spectrum appears incompatible with such a structure. Its lowest-wavelength maximum in the carbonyl region occurs at 1652 cm.$^{-1}$, whereas 1-(3-oxobut-1-enyl)ferrocene (II; R = CH:CH·CO·CH_3) prepared for comparison from the monoaldehyde and acetone has a peak at 1674 cm.$^{-1}$.



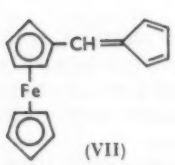
(IV)



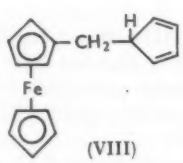
(V)



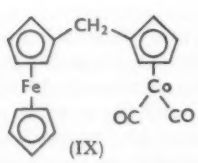
(VI)



(VII)



(VIII)



(IX)

We also performed some new reactions of the monoaldehyde (II; R = CHO). In addition to the methods previously recorded, this aldehyde has now been obtained, albeit in very low yield, by the McFadyen–Stevens [11] method from ferrocenecarboxylic acid (II; R = CO_2H). The aldehyde was reduced by the Clemmensen method to methylferrocene (II; R = Me), also obtained by Emde reduction of ferrocenylmethyltrimethylammonium iodide (II; R = $CH_2 \cdot NMe_3^+I^-$). While the present work was in progress, the latter method was described independently by Nesmeyanov *et al.*[12] who also obtained methylferrocene by reducing methyl ferrocenecarboxylate (II; R = CO_2Me) with a large

[11] McFadyen and Stevens, *J.*, 1936, 584.
[12] Nesmeyanov, Perevalova, Shilovtseva, and Beinoravichute, *Doklady Akad. Nauk S.S.S.R.*, 1958, **121**, 117.

excess of lithium aluminium hydride. Ferrocenecarboxyaldehyde undergoes Wittig condensation with allyltriphenylphosphinylide, giving ferrocenylbutadiene (VI). The aldehyde condenses with cyclopentadiene, to afford α-ferrocenylfulvene (VII). These two products are of interest as precursors of ferrocene-containing polymers. The closely related ferrocenylmethylcyclopentadiene (VIII) has been obtained by reaction of ferrocenylmethyltrimethylammonium iodide (II; R = CH_2·$NMe_3^+I^-$) with cyclopentadienylsodium and reacts readily with dicobalt octacarbonyl, the product being however rather unstable: although not obtained analytically pure, this undoubtedly has the expected structure (IX) and is a compound of novel type, containing two different transition metals in one molecule. Numerous examples of this type are being studied in our laboratories.

Experimental

Ligroin refers to the solvent of b. p. 60—80° unless otherwise specified. Alumina refers to Spence's grade " H " which had been exposed to air for 6 hr.

Dimethyl Ferrocene-1,1′-dicarboxylate.—Cyclopentadiene (6·6 g., 0·1 mole) in tetrahydrofuran (20 ml.) was added dropwise with stirring to powdered sodium (4·6 g.; 0·2 g.-atom) under the same solvent (50 ml.) in an atmosphere of nitrogen and the mixture was stirred for 1½ hr. A solution of methyl chloroformate (9·45 g., 0·1 mole) in tetrahydrofuran (20 ml.) was added dropwise, producing an immediate red colour. After a further 5 hours' stirring all the sodium had dissolved and anhydrous ferrous chloride (prepared from 20 g. of ferric chloride [13]) was added as a slurry in tetrahydrofuran, and the mixture stirred overnight. After removal of the solvent, the residue was extracted with benzene, and this extract concentrated and chromatographed on neutralised alumina. The main red material was eluted with benzene, recovered, and crystallised from ligroin, giving dimethyl ferrocene-1,1′-dicarboxylate (4·3 g., 28·5%), m. p. and mixed m. p. 107—109°.

1,1′-Diacetylferrocene.—The above procedure was repeated, but with acetyl chloride (7·85 g., 0·1 mole) in place of methyl chloroformate. 1,1′-Diacetylferrocene (0·55 g., 2%), identical in m. p. and mixed m. p. with an authentic sample, was isolated.

1,1′-Bis(dimethylaminomethyl)ferrocene (III; R = CH_2·NMe_2).—A solution of dimethylaminomethylferrocene (II; R = CH_2·NMe_2) (5·44 g., 0·02 mole) in anhydrous ethylamine (100 ml.) was poured on lithium metal (3·0 g., 0·43 g.-atom) as rapidly as the vigorous reaction permitted (in ~2 min.). The mixture was stirred for 20 min. and then poured on ferrous chloride [from ferric chloride (6 g., 0·04 mole)] tetrahydrofuran being used to rinse the original reaction vessel and added to the mixture which was then stirred at room temperature overnight. After removal of the solvents the residue was chromatographed in benzene on alumina. Three bands developed; benzene eluted ferrocene (0·59 g., 14·5%). This was followed by dimethylaminomethylferrocene (II; R = CH_2·NMe_2) (1·94 g., 36%; eluted with ether); and 1,1′-bis(dimethylaminomethyl)ferrocene (III; R = CH_2·NMe_2) (1·0 g., 15%) was eluted with acetone. The last was characterised as its picrate, m. p. 150° (decomp.), and *dimethiodide*, m. p. 260° (decomp.) (Found: C, 36·5, 37·6; H, 5·3, 5·4; N, 5·0. $C_{18}H_{30}FeI_2N_2$ requires C, 37·0; H, 5·2; N, 4·8%).

A similar experiment without ferrous chloride yielded 1·02 g. (18·2%) of the unchanged amine (II; R = CH_2·NMe_2); thus the initial decomposition was over 80% complete under these conditions.

The dimethiodide, on hydrolysis with 5N-sodium hydroxide at 180° for 3 hr. in a sealed tube, gave a low yield of the diol (III; R = CH_2·OH), m. p. and mixed m. p.[14] 107—108° (correct infrared spectrum).

Ferrocene-1,1′-dicarboxyaldehyde (III; R = CHO).—" Active " manganese dioxide (100 g.) was added to a solution of 1,1′-di(hydroxymethyl)ferrocene [4] (10 g.) in chloroform (200 ml.). The mixture became warm and was left in the dark for 12 hr. After filtration, the red solution was evaporated and the dry residue chromatographed in benzene on alumina. Benzene eluted *ferrocene-1,1′-dicarboxyaldehyde* (3·4 g., 34%) which formed bright red needles, m. p. 183—184°, from cyclohexane (Found: C, 59·4; H, 4·3. $C_{12}H_{10}FeO_2$ requires C, 59·5; H, 4·2%). A second band, eluted with ether, afforded *1′-hydroxymethylferrocene-1-carboxyaldehyde* which

[13] Kovacic and Brace, *J. Amer. Chem. Soc.*, 1954, **76**, 5491.

[14] Rinehart, Frerichs, Kittle, Westman, Gustafson, Pruett, and McMahon, *J. Amer. Chem. Soc.*, 1960, **82**, 4111.

crystallised from cyclohexane as orange plates (1 g., 10%), m. p. 39—40° (Found: C, 59·4; H, 5·1. $C_{12}H_{12}FeO_2$ requires C, 59·05; H, 5·0%). The *semicarbazone* of the latter formed orange crystals (from acetone), m. p. 166—167° (Found: C, 52·3; H, 5·4; N, 13·7. $C_{13}H_{15}FeN_3O_2$ requires C, 51·9; H, 5·0; N, 14·0%).

Ferrocene-1,1′-dialdoxime.—A solution of hydroxylamine hydrochloride (0·17 g.) in water (1 ml.) was added to a solution of ferrocene-1,1′-dicarboxyaldehyde in (0·08 g.) in ethanol (5 ml.). Sodium hydroxide (0·3 g.) was then added. The solution was refluxed for 1 hr., cooled, poured into water, and neutralised by solid carbon dioxide. The *dioxime* (0·06 g., 67%) was filtered off and recrystallised from benzene; it had m. p. 135° (Found: C, 52·3; H, 4·5; N, 10·1. $C_{12}H_{12}FeN_2O_2$ requires C, 53·0; H, 4·5; N, 10·3%).

1,1′-Dicyanoferrocene.—A solution of ferrocene-1,1′-dialdoxime (0·815 g., 1 mol.) and dicyclohexylcarbodi-imide (1·27 g., 2 mol.) in dry benzene (20 ml.) was refluxed for 15 hr. After cooling and removal of dicyclohexylurea (1·18 g., 90%), the solution was concentrated under reduced pressure. The remaining dinitrile was purified by chromatography on alumina in benzene and, crystallised from the same solvent, had m. p. 166—167° (lit.,[10] m. p. 166—167·5°) (0·70 g., 98%).

Condensation of the Dialdehyde with o-Phenylenediamine.—Ferrocene-1,1′-dicarboxyaldehyde (0·39 g.) and *o*-phenylenediamine (0·19 g.) were refluxed in ethanol for 2 hr. The solvent was removed *in vacuo*, the brown residue was dissolved in chloroform and chromatographed on alumina, and the only coloured band eluted with the same solvent. The orange-brown *compound* (IV?) (0·38 g.) obtained on evaporation did not crystallise but was purified by precipitation from chloroform with benzene as an orange powder, m. p. 210° (Found: C, 69·6; H, 4·95; N, 8·15. $C_{18}H_{14}FeN_2$ requires C, 68·8; H, 4·5; N, 8·9%).

Condensation of the Dialdehyde with Acetone.—Ferrocene-1,1′-dicarboxyaldehyde (0·49 g., 1 mol.), acetone (0·12 g., 1 mol.), and an excess of potassium hydroxide were refluxed in ethanol (20 ml.) for 1·5 hr. The precipitated purple solid (0·36 g.) was filtered off from the cooled mixture, washed with ethanol, and chromatographed in chloroform on alumina. Only one band was formed which, on elution, gave a deep purple crystalline *substance*, which did not melt below 300° and could not be recrystallised (Found: C, 64·1; H, 4·9; Fe, 19·7. $C_{15}H_{14}FeO_2$ requires C, 63·9; H, 5·0; Fe, 19·8%). The compound gave a positive iodoform test and showed strong maxima in the infrared at 1652, 1619, and 1587 cm.$^{-1}$.

1-(3-Oxobut-1-enyl)ferrocene.—Ferrocenecarboxyaldehyde (0·1 g.) and potassium hydroxide (0·1 g.), dissolved in water (1 ml.) and acetone (5 ml.), were refluxed for 1 hr. More water was added, the product extracted with benzene, and the dried extract concentrated to small bulk and then chromatographed on alumina. Unchanged aldehyde was eluted first, followed by the *ketone* which crystallised from ligroin in bright red plates, m. p. 85° (Found: C, 66·5; H, 5·6. $C_{14}H_{14}FeO$ requires C, 66·2; H, 5·6%). It gave a positive iodoform reaction and yielded a semicarbazone, m. p. 176°, $\nu_{max.}$ 1674, 1647, and 1622 cm.$^{-1}$.

Ferrocenecarboxyhydrazide (with G. D. Broadhead).—Methyl ferrocenecarboxylate (6 g., 1 mol.) and hydrazine hydrate (15 ml., 12 mol.) were refluxed in methanol (30 ml.) for 8 hr. Water was then added, the solution concentrated, and the *ferrocenecarboxyhydrazide* (4 g., 60%) which separated as orange-yellow plates recrystallised from methanol; it had m. p. 159—160° (Found: C, 54·4; H, 5·4. $C_{11}H_{12}FeN_2O_2$ requires C, 54·1; H, 5·4%).

N′-Benzenesulphonylferrocenecarboxyhydrazide.—Benzenesulphonyl chloride (0·22 g.) was added to the above hydrazide (0·30 g.) in pyridine (15 ml.). After 1 hr. at room temperature the mixture was poured on ice and hydrochloric acid, and the orange precipitate filtered off, washed with dilute hydrochloric acid and water, and dried. Crystallisation from chloroform afforded the *benzenesulphonyl derivative* (0·4 g., 85%), m. p. 203°, decomp. 222° [Found: C, 52·8; H, 4·3; N, 7·3; S, 8·5. $C_{17}H_{16}FeN_2O_3S$ requires: C, 53·1; H, 4·2; N, 7·3; S, 8·4%).

Ferrocenecarboxyaldehyde.—*N′*-Benzenesulphonylferrocenecarboxyhydrazide (0·164 g.) was heated in ethylene glycol (4 ml.) to 160°. An excess of sodium carbonate (0·12 g.) was then added in one portion, causing a brisk effervescence. The bath-temperature was maintained at 160° for 35 min. The mixture was then cooled, diluted with water, and extracted with ether, and the ether extract was washed with water, dried, and evaporated. The very small orange residue crystallised from light petroleum (b. p. 40—60°) and was identified as ferrocenecarboxyaldehyde by its m. p. and mixed m. p.

Methylferrocene.—Ferrocenecarboxyaldehyde (1 g.) in glacial acetic acid (20 ml.) was added to amalgamated zinc needles (7 g.) and concentrated hydrochloric acid (20 ml.) under nitrogen.

The mixture was heated on a steam bath for 15 min., cooled, and poured into water; the mixture was filtered and the solid material washed with benzene. The two layers in the filtrate were separated, the aqueous layer was extracted three times with benzene, and the combined benzene solutions were washed with water, aqueous sodium hydrogen carbonate, and water and dried (Na_2SO_4). Removal of benzene under reduced pressure left a yellow oil (0·8 g.), slightly volatile with benzene. Distillation of this oil at 86°/0·4 mm. afforded methylferrocene (0·6 g., 66%) which, crystallised from ligroin, had m. p. 36° undepressed by a sample obtained by reduction of ferrocenylmethyltrimethylammonium iodide with sodium and ethanol or sodium amalgam [11] (Found: C, 66·2; H, 6·1%; *M*, 204. Calc. for $C_{11}H_{12}Fe$: C, 66·0; H, 6·05%; *M*, 200).

1-(*Buta*-1,3-*dienyl*)*ferrocene* (VI).—As in Wittig and Haag's procedure,[15] allyltriphenylphosphonylide was obtained by addition of an excess of ethereal butyl-lithium to a suspension of allyltriphenylphosphonium bromide (2 g., 1 mol.) in ether (40 ml.). After this mixture has been stirred for 30 min., an ether solution of ferrocenecarboxyaldehyde (1·05 g., 1 mol.) was added and stirring continued overnight. Water was then added, the red ether layer separated, and the aqueous layer extracted with chloroform until colourless. The combined organic extracts were evaporated to dryness and a benzene solution of the residue was chromatographed on alumina. Unchanged aldehyde (0·5 g., 50%) was preceded on the column by 1-(*buta*-1,3-*dienyl*)*ferrocene* which distilled in a high vacuum and crystallised from ligroin (b. p. 40—60°) as red crystals (0·075 g., 12%), m. p. 80° (Found: C, 70·2; H, 6·0. $C_{14}H_{14}Fe$ requires C, 70·6; H, 5·9%).

α-*Ferrocenylfulvene* (VII).—Cyclopentadiene (1·0 g., 2 mol.) and ferrocenecarboxyaldehyde (1·6 g., 1 mol.), in ethanol (50 ml.), were added to a solution from sodium (2 g.) in ethanol (20 ml.). The mixture was heated on a steam bath for 30 min., then poured into water and extracted with ether. The ether extract was dried (Na_2SO_4) and evaporated, leaving a red oil which was chromatographed in benzene on alumina. Elution of the single coloured band with the same solvent afforded α-ferrocenylfulvene (1·9 g., 98%) as a deep red oil which polymerised on attempted distillation.

Ferrocenylmethylcyclopentadiene (VIII).—Ferrocenylmethyltrimethylammonium iodide (4·7 g., 1 mol.) was added to a solution of cyclopentadienylsodium prepared in tetrahydrofuran (50 ml.) from cyclopentadiene (4 g., 5 mol.) and an excess of powdered sodium. The mixture was stirred and refluxed under nitrogen for 15 hr. The solvent was removed *in vacuo*, and the residue treated with water and extracted with ether. The dried extract was evaporated and *ferrocenylmethylcyclopentadiene* (2·1 g., 65%) distilled at 104°/0·15 mm. as a mobile dark-red oil (Found: C, 72·6; H, 6·2. $C_{16}H_{16}Fe$ requires C, 72·8; H, 6·1%). The compound polymerised on storage, but the monomer was regenerated by distillation.

Dicarbonyl(*ferrocenylmethylcyclopentadienyl*)*cobalt* (IX).—A solution of the cyclopentadiene derivative (VIII) (0·9 g., 3·4 mol.) and dicobalt octacarbonyl (1·7 g., 5 mol.) in butyl ether (40 ml.) was refluxed for 1 hr. under nitrogen. The solvent was evaporated under a reduced pressure of nitrogen, and the residue extracted with benzene and chromatographed on alumina. A single red band was rapidly eluted with benzene. Removal of solvent left the product (IX) as a red oil (0·3 g., 13%) which decomposed gradually, was shown to contain cobalt, and had strong infrared maxima in the carbonyl–metal stretching region (2018 and 1962 cm.$^{-1}$).

The authors are indebted to the Minnesota Mining and Manufacturing Company for financial support and to E. I. du Pont de Nemours and Co. for gifts of ferrocene.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, April 10th*, 1961.]

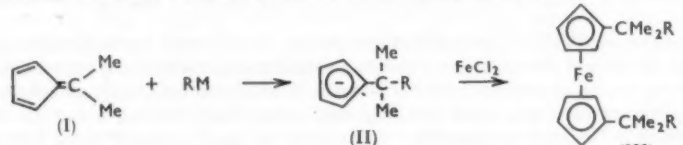
[15] Wittig and Haag, *Chem. Ber.*, 1955, **88**, 1654.

902. *Ferrocene Derivatives. Part X.*[1] *Their Preparation from Fulvenes.*[2]

By G. R. Knox and P. L. Pauson.

The conversion of fulvenes into substituted cyclopentadienide ions and thence by ferrous chloride into dialkyl- and alkenyl-ferrocenes is described. Azulene is shown to behave as a fulvene in these reactions.

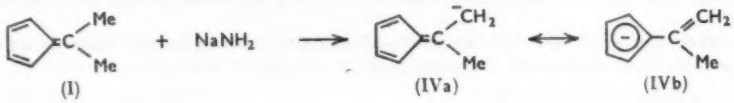
In Part I[3] the preparation of ferrocene from cyclopentadienyl-lithium (or the corresponding Grignard reagent) and iron halides was extended to aryl- and alkyl-cyclopentadienes. One of the routes to such starting materials is from the readily accessible fulvenes. In special cases[3,4] these may be reduced by metallic sodium or, more generally, by lithium aluminium hydride[5] to s-alkylcyclopentadienes. In the latter reaction the substituted cyclopentadienyl-lithium or lithium aluminium hydride derivative (II; M = Li or $LiAlH_3$, R = H) is a probable intermediate and it appeared likely that treatment with ferrous chloride would convert this directly into the ferrocene derivative, the necessity of isolating the free cyclopentadiene being thus avoided.



These expectations proved correct when dimethylfulvene (I) was treated with lithium aluminium hydride, followed by ferrous chloride, and di-isopropylferrocene (III; R = H) was isolated. Similarly 1,1′-dicyclohexylferrocene was obtained from pentamethylenefulvene (cyclopentadienylidenecyclohexane). The identification of " M " in this reaction as " $LiAlH_3$ " is suggested by the necessity of employing 1 mole of lithium aluminium hydride per mole of fulvene before the colour of the latter disappears.

The above formulation (I ⟶ II) has also been employed by Ziegler and Schäfer[6] for the addition of alkyl- or aryl-lithium to dimethylfulvene. Although these workers did not conclusively establish the structure of the product (II), this is adequately confirmed by its use in the present work to afford the 1,1′-di-t-alkylferrocenes (III; R = Me and Ph) by the above scheme (where M = Li). An analogous product was prepared from pentamethylenefulvene, phenyl-lithium, and ferrous chloride.

The quest for other anions (R^-) which might add in this way to fulvenes, led us to try sodamide, which was found to react in a different manner:



Dimethylfulvene and related compounds behave as acids towards this strong base. The acidity, as that of other cyclopentadiene derivatives, may be ascribed to the formation

[1] Part IX, preceding paper.
[2] For a preliminary communication see *Proc. Chem. Soc.*, 1958, 289
[3] Pauson, *J. Amer. Chem. Soc.*, 1954, **76**, 2187.
[4] Schlenk and Bergmann, *Annalen*, 1928, **463**, 1.
[5] Ziegler, Gellert, Martin, Nagel, and Schneider, *Annalen*, 1954, **589**, 91.
[6] Ziegler and Schäfer, *Annalen*, 1934, **511**, 101.

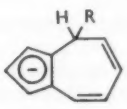
of the resonance-stabilised cyclopentadienide ion (IVb) which in this case has an additional canonical form (IVa). In other words, the acidity of fulvenes follows from that of cyclopentadiene itself by the principle of vinylogy. This consideration suggested further extension to such fulvenes as (V) and indeed this reacted readily with sodamide, presumably yielding the anion (VI). The only previous evidence for the acidity of fulvenes appears to be that Schlenk and Bergmann [7] observed the formation of triphenylmethane from dimethylfulvene and triphenylmethylsodium.

The anions (*e.g.*, IV and VI) produced with sodamide reacted smoothly with ferrous chloride, to give ferrocene derivatives bearing unsaturated side chains. These are rather difficult to isolate owing to the great ease with which they polymerize. For instance, Riemschneider and Helm [8] were unable to isolate di-isopropenylferrocene when it was prepared by another method. In the present work we were able to obtain this compound from the ion (IV) and ferrous chloride, albeit in low yield and accompanied by much polymer. Similar results were obtained when pentamethylenefulvene was employed as starting material to yield 1,1′-dicyclohex-1-enylferrocene. The structure of the latter was verified by reduction to dicyclohexylferrocene and dehydrogenation to the known diphenylferrocene; diphenylferrocene was also reduced to the dicyclohexyl derivative.

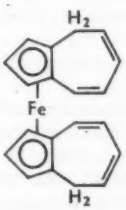
When, however, methylfulvene or propenylfulvene (V) was employed, the isolation of the expected divinyl- and dibutadienyl-ferrocene did not prove possible although polymeric ferrocenes which must clearly be derived from these products resulted. The low stability of the monomer is in contrast to the ready isolation of monovinyl- [9,10] and monobutadienyl-ferrocene [1] and suggests that the proximity of the unsaturated side chains assists polymerisation. It appears likely, therefore, that the polymers of, *e.g.*, divinylferrocene are of the form (VII) containing bridged rings.

(VII) $-CH_2-CH(C_5H_4-Fe-C_5H_4)-CH_2-CH(C_5H_4-Fe-C_5H_4)-CH_2-CH_2-$

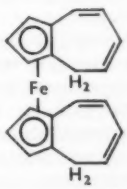
Azulene was included in the present study, since formally it contains a fulvene system. Hafner and Weldes [11] have shown that it adds alkyl-lithium, affording 4-alkyl-3α,4-dihydroazulenes, presumably by way of anions of type (VIII). Direct treatment with ferrous chloride converted these intermediates into the corresponding ferrocenes. A mixture of six stereoisomers (four racemates and two *meso*-forms) is theoretically possible, and not surprisingly a pure substance was not obtained when phenyl-lithium was employed. When R = H only two such isomers (1 *meso*, 1 racemic) are possible. This required addition of a hydride to azulene and although such additions had not been described,



(VIII)



(IXa)



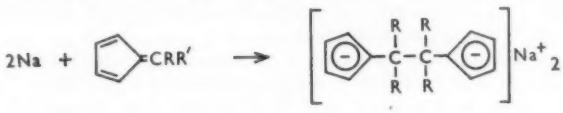
(IXb)

lithium aluminium hydride again proved successful though it added much more slowly than to fulvenes. From the oily product one component was isolated with m. p. 68°, but a sample with the melting range 47—53°, presumably containing both expected

[7] Schlenk and Bergmann, *Annalen*, 1930, **479**, 58.
[8] Riemschneider and Helm, *Chem. Ber.*, 1956, **89**, 155.
[9] Arimoto and Haven, *J. Amer. Chem. Soc.*, 1955, **77**, 6295.
[10] Hauser, Lindsay, and Lednicer, *J. Org. Chem.*, 1958, **23**, 358.
[11] Hafner and Weldes, *Annalen*, 1957, **606**, 90.

isomers (IXa and b), gave analyses in agreement with this composition and was characterised by hydrogenation to its octahydro-derivative.

After completion of the present work, Pruett and his co-workers [12] described an alternative use of fulvenes, which leads to bridged ferrocenes and is apparently based on the dimerisation of fulvenes by alkali metals first reported by Schlenk and Bergmann.[4]



Experimental

Unless otherwise stated, ligroin refers to the solvent of b. p. 60—80°. Alumina refers to Spence's grade H which had been exposed to air for 6 hr.

M. p.s were determined in sealed evacuated capillaries.

Ferrous chloride (anhydrous) employed in this and the following papers was freshly prepared by the method of Kovacic and Brace.[13]

1,1′-*Di-t-butylferrocene*.—Dimethylfulvene (2·12 g., 0·02 mole) in ether (10 ml.) was added to methyl-lithium, prepared in a nitrogen atmosphere from lithium (0·33 g., 0·05 g.-atom) and methyl iodide (3·15 g., 0·0248 mole). The mixture was stirred for 0·5 hr., ferric chloride (1·625 g., 0·01 mole) in ether (20 ml.) was added to the pale yellow precipitate to produce a blue mixture, and stirring was maintained for a further 2·5 hr. The ferricenium salt mixture was poured on ice (100 g.) and 12·5% titanous chloride solution (100 ml.), and the red-yellow ethereal solution was removed and dried over anhydrous sodium sulphate and zinc dust. Removal of the solvent in a nitrogen atmosphere afforded an oil (3·65 g.), which was chromatographed on alumina with ligroin as solvent; the eluate was evaporated, yielding a red-brown oil (2·8 g., 94%). 1,1′-Di-t-butylferrocene is an orange liquid, b. p. 108° (bath)/0·05 mm., $n_D^{21·5}$ 1·550 (Found: C, 72·85; H, 8·8. Calc. for $C_{18}H_{26}Fe$: C, 72·6; H, 8·7%).

After our work,[2] Riemschneider and Nehring [14] prepared this compound, with m. p. 29—30°, from t-butylcyclopentadiene.

1,1′-*Di-*(α*α-dimethylbenzyl*)*ferrocene*.—Phenyl-lithium was prepared in ethereal solution (30 ml.) from lithium (0·33 g., 0·05 g.-atom) and bromobenzene (3·5 g., 0·021 mole), under nitrogen. Dimethylfulvene (2·12 g., 0·02 mole) in ether (10 ml.) was added dropwise, to produce a pale cream-coloured precipitate. Anhydrous ferric chloride (1·625 g., 0·01 mole) in ether (20 ml.) was added to the rapidly stirred suspension, and the mixture stirred for 2 hr., then poured on ice (100 g.), concentrated hydrochloric acid (2 ml.), and 12·5% titanous chloride solution (50 ml.). The organic material was separated with chloroform (150 ml.), washed with water, dried ($CaCl_2$), and evaporated, to leave a dark red oil (3·50 g., 83%) which solidified. Recrystallisation from ligroin–benzene afforded orange rods of 1,1′-*di-*(α*α-dimethylbenzyl*)-*ferrocene* (2·4 g., 57%), m. p. 133·5—134° (Found: C, 79·6; H, 7·3. $C_{28}H_{30}Fe$ requires C, 79·6; H, 7·2%).

In a similar reaction the use of anhydrous ferrous chloride and tetrahydrofuran increased the yield of crude material to 90%.

1,1′-*Di-*(1-*phenylcyclohexyl*)*ferrocene*.—Pentamethylenefulvene (cyclopentadienylidenecyclohexane) [15] (b. p. 118°/18 mm.; 2·92 g., 0·02 mole) in ether (15 ml.) was added dropwise to a stirred solution of phenyl-lithium (0·02 mole) in ether (30 ml.), under nitrogen, at a rate such that gentle refluxing was maintained. After 45 min. ferrous chloride [prepared from ferric chloride (3·3 g., 0·02 mole)] as a slurry in tetrahydrofuran (25 ml.) was added to the cream-coloured precipitate. The mixture was stirred under nitrogen at room temperature for 16 hr., poured into water (150 ml.) and titanous chloride solution (25 ml.), and extracted with ether (2 × 50 ml.). The combined ether extracts were washed with water (2 × 100 ml.), dried ($CaCl_2$), and evaporated to a brown oil (5·1 g., 100%) which solidified. Three recrystallisations

[12] Union Carbide, Belgian P. 563,103; Ger. P. 1,052,401; Rinehart, Frerichs, Kittle, Westman, Gustafson, Pruett, and McMahon, *J. Amer. Chem. Soc.*, 1960, **82**, 4111.
[13] Kovacic and Brace, *J. Amer. Chem. Soc.*, 1954, **76**, 5491.
[14] Riemschneider and Nehring, *Monatsh.*, 1959, **90**, 568.
[15] Kohler and Kable, *J. Amer. Chem. Soc.*, 1935, **57**, 917.

from ligroin gave orange-brown prisms of 1,1′-*di*-(1-*phenylcyclohexyl*)*ferrocene* (4·9 g., 96%), m. p. 135—136° (Found: C, 81·4; H, 7·8. $C_{34}H_{38}Fe$ requires C, 81·3; H, 7·6%).

1,1′-*Dicyclohexylferrocene*.—Pentamethylenefulvene (2·92 g., 0·02 mole) in ether (10 ml.) was added dropwise, under nitrogen, to a stirred suspension of lithium aluminium hydride (0·76 g., 0·02 mole) in ether (10 ml.). A vigorous reaction ensued, and a thick white precipitate was formed. A solution of anhydrous ferric chloride in ether was added dropwise to the mixture until a permanent (10 min.) blue colour developed. The mixture was added to ice-water (100 ml.) and 12·5% titanous chloride solution (50 ml.) and extracted with ether (3 × 50 ml.). The combined ether extracts were dried ($CaCl_2$) and evaporated to an orange oil (2·0 g.) which rapidly became green in air. Ligroin (50 ml.) and zinc dust were added to the oxidised material, and the mixture was shaken for 0·5 hr., filtered, and chromatographed on alumina. The main orange band was eluted rapidly with ligroin, the eluent evaporated under a reduced atmosphere of nitrogen, and the residue distilled at 184° (bath)/0·08 mm. 1,1′-*Dicyclohexylferrocene* (1·8 g., 77%) crystallised as fine orange-brown rods, m. p. 42·5°. The m. p. remained unchanged after six further distillations (Found: C, 76·6; H, 8·55. $C_{22}H_{30}Fe$ requires C, 75·4; H, 8·6%).

Solid 1,1′-dicyclohexylferrocene is stable in air but in solution the substance was oxidised, and owing to its great solubility in organic solvents did not recrystallise satisfactorily.

Catalytic Hydrogenation of 1,1′-*Diphenylferrocene*.—1,1′-Diphenylferrocene (0·1014 g., 0·0003 mole) was added in ether (15 ml.) to 10% palladium–charcoal (20 mg.; presaturated with hydrogen) in ether (10 ml.). After 16 hr. 5 ml. of hydrogen had been absorbed (theor. 3 ml.), and the ethereal solution was practically colourless. Continuous ether-extraction of the catalyst and evaporation of the extract left an orange oil (0·142 g.), which crystallised. Chromatography of this solid in ligroin yielded 1,1′-dicyclohexylferrocene (0·07 g., 66·7%), m. p. 42—43° after a single distillation. The other products were not investigated.

1,1′-*Di-isopropylferrocene*.—Dimethylfulvene (2·12 g., 0·02 mole) in ether (25 ml.) was added dropwise to a stirred suspension of lithium aluminium hydride (0·19 g., 0·02 mole) in ether (10 ml.) at room temperature under an atmosphere of nitrogen. After 15 min., anhydrous ferric chloride (1·625 g., 0·01 mole) in ether (40 ml.) was added dropwise, and the resulting blue mixture stirred for a further 12 hr. at room temperature, then poured on ice (100 g.) and titanous chloride solution (200 ml.). The organic phase was separated, combined with the ether extracts (3 × 100 ml.), dried, and evaporated. The residual oil (2·91 g.), after chromatography, gave 1,1′-*di-isopropylferrocene* (2·0 g., 74%) as an orange-red liquid, b. p. 91°/0·025 mm., n_D^{20} 1·5604 (Found: C, 71·55; H, 8·0. $C_{16}H_{22}Fe$ requires C, 71·1; H, 8·2%).

Reaction between Azulene, Phenyl-lithium, and Ferrous Chloride.—Azulene (2·56 g., 0·02 mole) in ether (25 ml.) was added to phenyl-lithium (*ca.* 0·02 mole) in ether (30 ml.), and the mixture stirred under nitrogen for 4 hr. at room temperature. Decolorisation was not complete. Ferrous chloride [from ferric chloride (4·875 g., 0·03 mole)], added in tetrahydrofuran (10 ml.) to the brown mixture, caused an immediate exothermic reaction and colour change to burgundy-red. After 13 hr. the mixture was filtered, and the solid residue washed with ether (50 ml.) and methanol (15 ml.), and digested with chloroform (2 × 50 ml.) at room temperature. The combined filtrate and organic phases were washed, dried ($CaCl_2$), and evaporated to a dark red oil (4·66 g., 100%). About 0·6 g. of this oil was dissolved in ligroin (10 ml.) and benzene (5 ml.) and placed on alumina (130 × 2 cm.). Elution with ligroin (900 ml.) removed a trace of azulene, followed by a diffuse pink band, whose ingredients were not separated. Evaporation left an oil, presumably containing the mixed isomers of di-(8,9-dihydro-8-phenylazulenyl)-iron(II). Sublimation did not succeed, but the residue, on trituration with ligroin, gave a solid, m. p. 103—107° (Found: C, 81·4; H, 5·9. $C_{32}H_{26}Fe$ requires C, 82·4; H, 5·6%).

Bis-(3α,4-*dihydroazulenyl*)*iron* (IX).—Azulene (1·28 g., 0·01 mole) and lithium aluminium hydride (0·40 g., *ca.* 0·01 mole) were suspended in ether (50 ml.; dried by lithium aluminium hydride) under nitrogen and the whole was shaken for 60 days. To the resulting colourless solution (which contained a brown suspension) was added anhydrous ferrous chloride [from anhydrous ferric chloride (1·625 g., 0·01 mole)] in tetrahydrofuran (100 ml.). An exothermic reaction took place and the mixture became red. After 36 hr. under nitrogen, methanol (10 ml.) was added and the mixture filtered and added to water (100 ml.). The dried organic phase was evaporated, the residue passed in benzene down a column of alumina, and the residue of the red mobile band rechromatographed on alumina (25 × 2·5 cm. column) in ligroin (b. p. 40—60°). Azulene (0·16 g.) was recovered from the first band. The second band was

not resolved by slow elution and yielded a red solid (0·52 g., 17%). This was twice recrystallised from ligroin (b. p. 40—60°) and twice sublimed at 60°/0·02 mm., the sublimate being washed with ligroin and recrystallised from the same solvent, to yield red needles of one isomer of bis-(3α,4-dihydroazulenyl)iron (IX), m. p. 68°. The mother liquors from the first recrystallisation were evaporated, and the residue was sublimed. The oily sublimate was partially resublimed twice, the most volatile fraction being retained each time; this finally yielded material, m. p. 18°, which did not crystallise when seeded with a crystal of the higher-melting isomer. A sample of the mixed isomers, having m. p. 47—53°, gave the expected analyses (Found: C, 76·4; H, 6·2. Calc. for $C_{20}H_{18}Fe$: C, 76·45; H, 5·8%).

Bis(hexahydroazulenyl)iron(II).—The crude mixed isomers of bis-(3α,4-dihydroazulenyl)-iron(II) (*ca.* 0·07 g.) were rapidly hydrogenated in methanol over Adams catalyst, changing in colour from red to yellow. The solution was filtered and evaporated. The residue was recrystallised twice from absolute ethanol, yielding golden-orange prisms of *bis(hexahydro-azulenyl)iron*, m. p. 52—54° (Found: C, 74·8; H, 8·3. $C_{20}H_{26}Fe$ requires C, 74·5; H, 8·1%).

1,1′-*Di-isopropenylferrocene*.—Sodamide was prepared from sodium (1·38 g., 0·06 g. atom) and liquid ammonia (150 ml.) containing a trace of ferric nitrate. Dimethylfulvene (6·36 g., 0·06 mole) was added, and the mixture stirred under nitrogen at the temperature of refluxing ammonia, assuming in 3 hr. a dark red colour. Anhydrous ferrous chloride [from ferric chloride (3·47 g., *ca.* 0·02 mole)] was added portionwise. The mixture was stirred for a further 18 hr. under nitrogen. The ammonia was allowed to evaporate, and ethanol (50 ml.), ice (150 g.), and ligroin (100 ml.; b. p. 40—60°) were added; the ligroin phase was separated, and the aqueous phase extracted with ligroin (3 × 100 ml.; b. p. 40—60°). The combined extracts were dried by passage down a column of calcium chloride and sodium sulphate, evaporated to small volume *in vacuo* at room temperature, and immediately chromatographed on alumina. The eluate of the main orange-red band, which was eluted after a small quantity of dimethylfulvene, was concentrated to small volume *in vacuo* at room temperature, rapidly filtered, and cooled to −70°. Orange-red crystals of 1,1′-*di-isopropenylferrocene* separated. An analytically pure sample had m. p. 58—59° after one recrystallisation (Found: C, 72·35; H, 7·0. $C_{16}H_{18}Fe$ requires C, 72·2; H, 6·8%). The material polymerised extremely rapidly in solution, and in contact with air in the solid state. Consequently yields varied considerably; they never exceeded 65%.

1,1′-*Dicyclohex*-1-*enylferrocene*.—Pentamethylenefulvene (4·38 g., 0·03 mole; n_D^{21} 1·568) was added to sodamide [from sodium (0·69 g.) and ferric nitrate] in liquid ammonia (150 ml.). After 4·5 hr. the mixture had assumed a dark red colour, and ferrous chloride [from anhydrous ferric chloride (4·95 g.)] was added portionwise in 10 min. The mixture was stirred for 13·5 hr. under nitrogen as the ammonia evaporated, then treated with ethanol (50 ml.), poured into water (500 ml.), and extracted with ether (4 × 100 ml.). The combined ether extracts were dried (soda-lime) and evaporated under a reduced pressure of nitrogen. The residue was chromatographed in ligroin (b. p. 40—60°) on alumina (20 × 3 cm.). The largest, first, orange band was eluted with the same solvent, the eluate filtered and evaporated (under nitrogen), and the residual red oil (3·7 g., 71%) distilled. The excess of pentamethylenefulvene distilled first, followed by 1,1′-*dicyclohex*-1-*enylferrocene*. This redistilled at 180° (bath)/0·15 mm., as a deep red oil, n_D^{24} 1·6215, which crystallised *in vacuo* as red prisms, m. p. 44° (Found: C, 75·8; H, 7·5. $C_{22}H_{26}Fe$ requires C, 76·3; H, 7·6%). Although polymerising rapidly in solution, or when an oil, solid 1,1′-dicyclohex-1-enylferrocene (unlike 1,1′-di-isopropenylferrocene) was unchanged in appearance after storage for six months in a sealed bottle.

Catalytic Hydrogenation of 1,1′-*Dicyclohex*-1-*enylferrocene*.—Freshly distilled 1,1′-dicyclohex-1-enylferrocene (*ca.* 0·85 g., 0·00246 mole) was hydrogenated overnight in pure ether (25 ml.) and over 10% palladium–charcoal (57 mg.). The solution was filtered, the catalyst washed with ether (5 × 10 ml.), and the filtrate evaporated to an orange oil (0·69 g.) which was distilled [b. p. 160° (bath)/0·07 mm.]. The distillate cooled to orange-brown needles, m. p. 39°; a mixed m. p. with 1,1′-dicyclohexylferrocene prepared from lithium aluminium hydride, pentamethylenefulvene, and anhydrous ferric chloride, was 42°.

Dehydrogenation of 1,1′-*Dicyclohex*-1-*enylferrocene*.—1,1′-Dicyclohex-1-enylferrocene (*ca.* 1·0 g., 0·003 mole) was heated with 10% palladium–charcoal (*ca.* 300 mg.) at 220—240° under nitrogen for 5·25 hr. Loss of material by sublimation was prevented by employing a water-condenser (100 cm.) plugged with cotton wool. The mixture was allowed to cool and extracted with

ether, and the extract was filtered and evaporated. The red oil (0·85 g.) was chromatographed in ligroin on alumina (44 × 2·5 cm.). Two bands developed, yielding successively unchanged 1,1′-dicyclohex-1-enylferrocene and 1,1′-diphenylferrocene. A single recrystallisation from ligroin gave 1,1′-diphenylferrocene (0·39 g., 40%) as red plates, m. p. and mixed m. p. 153—154°.

The authors thank the D.S.I.R. for a maintenance grant (to G. R. K.) and Esso Research Ltd. for a gift of cyclopentadiene.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, April 10th*, 1961.]

903. *Ferrocene Derivatives. Part XI.*[1] *Azoferrocenes.*[2]

By G. R. KNOX and P. L. PAUSON.

Successive treatment with methyl- or phenyl-lithium and ferrous chloride converts diazocyclopentadiene into 1,1′-dimethyl(or phenyl)azoferrocene, reducible to 1,1′-diaminoferrocene. Extension of this synthesis to monophenylazoferrocene is described.

AMINOFERROCENE has been prepared by two routes. Nesmeyanov *et al.*[3] obtained it by metallation of ferrocene with butyl-lithium followed by treatment with *O*-benzylhydroxylamine (Kochetkov reaction). Although the first step is known [4] to lead to a mixture of mono- and di-substitution products, only the monoamine has been reported as formed by this procedure. Arimoto and Haven [5] prepared the same amine by Curtius degradation of ferrocenecarboxylic acid. An earlier attempt [6] to employ this method for the preparation of 1,1′-diaminoferrocene (I; R = H) had yielded the intermediate urethanes (I; R = CO·OEt and CO·O·CH_2Ph), but attempts to convert them into the free amines caused complete destruction.

Aminoferrocene proved very sensitive to oxidation and was completely destroyed by nitrous acid, no diazonium salt being detectable.[3] Moreover, it was shown in Part II [7] that, unlike other aromatic systems of comparable reactivity, ferrocene fails to couple with diazonium salts but, instead, undergoes arylation by such salts.

Extension of the reactions described in the preceding paper [1] to diazocyclopentadiene [8] (II) has now provided a direct route to alkyl- and aryl-azoferrocenes, inaccessible by the more conventional methods referred to above; and reduction of these azo-derivatives then afforded both the mono- and the 1,1′-diamino-derivative.

Organometallic compounds are known to add to diazomethane, giving the corresponding metal salts of azo-compounds, $M^{+-}CH_2{\cdot}N{:}NR$, which on hydrolysis commonly yield substituted hydrazones, $CH_2{:}N{\cdot}NHR$.[9]

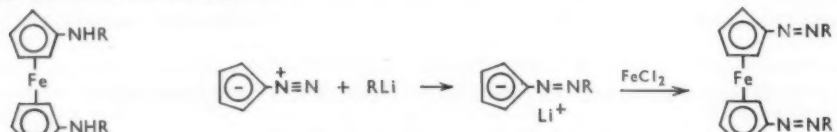
As expected, phenyl-lithium added similarly to diazocyclopentadiene. The initial product, the phenylazocyclopentadienyl ion (cf. III; R = Ph), was treated with ferrous chloride, affording diphenylazoferrocene (IV; R = Ph). Use of methyl-lithium similarly afforded dimethylazoferrocene (IV; R = Me).

Use of a mixture of the lithium salt (III; R = Ph) with unsubstituted cyclopentadienyl-lithium afforded the monosubstituted derivative, phenylazoferrocene (V).

When this product (V) was hydrogenated over Adams catalyst in methanol uptake of hydrogen was only ~ 1 mol. The resultant orange solution rapidly reverted to the

[1] Part X, preceding paper.
[2] For a preliminary communication see Knox, *Proc. Chem. Soc.*, 1959, 56.
[3] Nesmeyanov, Perevalova, Golovnya, and Shilovtseva, *Doklady Akad. Nauk S.S.S.R.*, 1955, **102**, 535.
[4] Benkeser, Goggin, and Schroll, *J. Amer. Chem. Soc.*, 1954, **76**, 4025.
[5] Arimoto and Haven, *J. Amer. Chem. Soc.*, 1955, **77**, 6295.
[6] Rosenblum, Thesis, Harvard, 1953.
[7] Broadhead and Pauson, *J.*, 1955, 367.
[8] Doering and De Puy, *J. Amer. Chem. Soc.*, 1953, **75**, 5955.
[9] Kharasch and Reinmuth, "Grignard Reactions of Non-metallic Substances," Constable, London, 1954, p. 1223.

purple colour of the starting material (V) in air. On account of its extreme sensitivity to air, no attempt was made to isolate the phenylhydrazoferrocene which is undoubtedly present in these solutions. Use of acetic acid as solvent permitted hydrogenation of the azo-compound (V) to aminoferrocene. This was identified by its melting point and by conversion into the methoxycarbonylamino-derivative, identical with a sample kindly supplied by Dr. K. Schlögl.



The behaviour of 1,1′-diphenylazoferrocene (IV) on hydrogenation in methanol and acetic acid was analogous. In the latter solvent, 1,1′-diaminoferrocene was undoubtedly obtained since treatment of the crude product with the appropriate alkyl chlorocarbonate yielded the urethanes (I; R = CO·OMe, CO·OEt, and CO·O·CH_2Ph), of which the last two agreed in m. p. with the samples previously reported.[6] In the first case, the presence of methyl carbanilate was also demonstrated and, together, these products provide good confirmation of the structure of the initial azo-compound (IV; R = Ph). The dimethylazo-compound (IV; R = Me) was reduced similarly and in this case complete evaporation of the filtered reaction mixture left the diamine as a yellow solid. Owing to its extreme sensitivity to air it has not been characterised.

Experimental

For general remarks see preceding paper.

1,1′-Diphenylazoferrocene.—Diazocyclopentadiene, prepared by the method of Doering and De Puy,[8] was distilled three times and used immediately. The yields after such purification varied between 20% and 40%. Diazocyclopentadiene (5·25 g., 0·06 mole) in ether (40 ml.) was added dropwise during 0·5 hr. to a solution of phenyl-lithium (0·06 mole) in ether (100 ml.), stirred at −30° under nitrogen. The resulting scarlet precipitate was treated with ferrous chloride [from ferric chloride (9·8 g., *ca.* 0·06 mole)] and tetrahydrofuran (45 ml.), producing an immediate change in colour to dark purple. After 14 hr. the temperature of the mixture had risen to 20°, and a black precipitate had been produced. The mixture was added to water (150 ml.), and the ether layer removed, washed with water (4 × 100 ml.), and dried (Na_2SO_4). The contents of the reaction vessel and the aqueous layer were extracted with benzene (5 × 150 ml.), and the deep red extracts washed, dried, evaporated, and combined with the residue from the evaporation of the ether extracts. The oily residue was dissolved in acetone, evaporated to about 200 ml., and cooled, yielding violet-black needles of *1,1′-diphenylazoferrocene* (6·8 g.), m. p. 170°. Concentration of the liquors to 20 ml. gave a further quantity (2·6 g.; total yield 80%) of crystalline material having a similar m. p. A sample for analysis was purified by chromatography on alumina in benzene, and by recrystallisation six times from pure acetone to a constant m. p. 183—185° (Found: C, 67·0; H, 4·9; N, 14·1. $C_{22}H_{18}FeN_4$ requires C, 67·0; H, 4·6; N, 14·2%).

Phenylazoferrocene.—Cyclopentadienyl-lithium was prepared in ether (250 ml.) from bromobenzene (43·2 g., 0·275 mole), lithium (4·07 g., 0·59 g.-atom), and cyclopentadiene (16·3 g., 0·25 mole). It was then added to phenylazocyclopentadienyl-lithium, prepared by stirring diazocyclopentadiene (7·65 g., 0·083 mole) and phenyl-lithium [from bromobenzene (14·4 g., 0·092 mole) and lithium (1·36 g., 0·195 g.-atom)] in ether (120 ml.) at −30° for 45 min. All

operations were conducted under nitrogen. The mixture was left for 0·5 hr., and ferrous chloride [from ferric chloride (35 g., 0·215 mole)] in tetrahydrofuran (50 ml.) then added. Stirring was continued for 14 hr., while the temperature rose to 23°. The mixture was added to ice-water (500 ml.). The ether layer was removed and combined with ether extracts (5 × 250 ml.), dried (Na_2SO_4), and evaporated, and the sticky residual solid dissolved in ligroin (b. p. 40—60°). The solution was chromatographed on alumina (70 × 5·5 cm.), ligroin (b. p. 40—60°) developing a total of ten coloured bands, of which the very minute bands IV, V, VII, VIII, and IX were rejected. Band I yielded ferrocene (19·0 g., 82·8% based on cyclopentadiene). Band II, also yellow-orange, gave an oil (0·79 g.), which solidified after distillation at 88—90° (bath)/0·05 mm., giving azobenzene, m. p. 65° with previous softening (mixed m. p. 67—68°) (Found: C, 78·8; H, 5·7. Calc. for $C_{12}H_{10}N_2$: C, 79·1; H, 5·5%). A separate experiment suggested that this product arises from toluene-*p*-sulphonyl azide, present as a contaminant in the diazocyclopentadiene, by reaction with phenyl-lithium. Band III, a very pale yellow, yielded an orange oil (0·89 g.) from which biphenyl was sublimed. Band VI on elution, concentration, and cooling, gave violet needles of *phenylazoferrocene* (3·9 g., 5·5% based on cyclopentadiene) which, recrystallised from ligroin, had m. p. 109—110° (Found: C, 65·9; H, 5·1; N, 9·6. $C_{16}H_{14}FeN_2$ requires C, 66·2; H, 4·9; N, 9·7%). The last band was extruded from the top of the column and extracted from the alumina with acetone, from which 1,1′-diphenylazoferrocene (2·4 g., 14·65%), m. p. 172—180°, crystallised.

1,1′-Dimethylazoferrocene.—Diazocyclopentadiene (2·76 g., 0·03 mole) in ether (10 ml.) was added dropwise to methyl-lithium (0·03 mole) in ether (25 ml.), stirred at room temperature under nitrogen. Ferrous chloride [from ferric chloride (4·9 g., *ca.* 0·03 mole)] was added in tetrahydrofuran (50 ml.) after 0·25 hr. The mixture was stirred at room temperature for 14 hr., poured into water (50 ml.), and extracted with an additional 100 ml. of ether, and the combined ether extracts were washed with water (3 × 20 ml.) and dried (Na_2SO_4). The residue in the flask was treated with methanol (10 ml.) and water (50 ml.) and extracted with chloroform (2 × 50 ml.). The washed and dried chloroform extracts were evaporated, and the residues combined with the material from the ether extracts, giving a red oil (1·44 g.) which was passed in ligroin down a column of neutral alumina (30 × 3 cm.). The eluate yielded a red oil (1·05 g., 26%). *1,1′-Dimethylazoferrocene* was purified by recrystallisation from ligroin (b. p. 40—60°) and sublimation at 65°/0·005 mm., forming maroon-coloured needles, m. p. 101—103° (with previous softening) (Found: C, 53·5; H, 5·3; N, 21·0. $C_{12}H_{14}FeN_4$ requires C, 53·35; H, 5·2; N, 20·7%).

Hydrogenation of Phenylazoferrocene.—(a) *With Adams catalyst in glacial acetic acid.* Phenylazoferrocene (0·299 g.) in glacial acetic acid (20 ml.) was added to Adams catalyst (43·5 mg.; presaturated with hydrogen) in glacial acetic acid (5 ml.). Hydrogenation for 14 hr. at 21°/755 mm. resulted in the theoretical absorption (55 ml.). The orange solution was filtered and then evaporated under a reduced pressure of nitrogen, benzene (25 ml.) added, the brown benzene solution shaken with sodium hydrogen carbonate solution (4 × 50 ml.), then water (2 × 50 ml.), dried (Na_2SO_4), and evaporated to an orange oil (0·2 g.) which solidified on cooling. A fraction of the crude material (0·15 g.) was sublimed at 80°/0·0003 mm., yielding orange-yellow aminoferrocene (0·075 g.), m. p. 151—153° (lit.,[3] m. p. 153—155°).

(b) *With Adams catalyst in anhydrous methanol.* Phenylazoferrocene (0·295 g.) in methanol (35 ml.) was added to Adams catalyst (12·0 mg.; presaturated with hydrogen) in anhydrous methanol (4 ml.), and the flask surrounded by aluminium foil to keep out light. Hydrogen absorption had ceased after 40 hr. (40 ml. at 21°/760 mm.) and the solution had changed colour from violet to orange. On filtration the solution became violet at once, but could be re-hydrogenated without difficulty. Exposure to air for less than 5 sec. was sufficient to cause partial oxidation. A specimen of the hydrogenation mixture, when kept under hydrogen, was unchanged after 3 months and had deposited orange crystals of, presumably, phenylhydrazoferrocene.

Methoxycarbonylaminoferrocene.—Phenylazoferrocene (0·275 g.) in presence of Adams catalyst (12 mg. of known activity) was hydrogenated in acetic acid (10 ml.) overnight, resulting in the absorption of 45 ml. of gas (21°/750 mm.). The solution was filtered rapidly and evaporated *in vacuo* on a steam bath, the residue dissolved in dry benzene (10 ml.), and the solution saturated with nitrogen. Methyl chloroformate (1 ml.) was added, immediately producing a black precipitate. Sodium hydrogen carbonate solution (3 × 5 ml.) was added after 0·5 hr., and the benzene layer was separated, washed with sodium hydrogen carbonate

solution (6 × 20 ml.) and water (4 × 50 ml.), dried, and evaporated. The residual yellow oil (0·325 g.) crystallised from water–methanol (0·5 : 2 ml.) at 0° as fine yellow needles (0·2 g., 80%), m. p. 126—138°. Further recrystallisation gave a sample, m. p. 138—142°, mixed m. p. with an authentic sample of methoxycarbonylaminoferrocene [10] 142—144°.

Hydrogenation of 1,1′-Diphenylazoferrocene.—(a) *With Adams catalyst in glacial acetic acid.* 1,1′-Diphenylazoferrocene (0·197 g.) in glacial acetic acid (5 ml.) and Adams catalyst (16·1 mg.) in acetic acid (5 ml.; pre-saturated with hydrogen) were stirred with hydrogen in the absence of light. Absorption was rapid (48 ml. at 21·3°/760 mm. in 2 hr.) (theor., 48·5 ml.). The solution had become orange, and yielded an orange oil on evaporation of the solvent at a reduced pressure of nitrogen. Air-free sodium hydrogen carbonate solution (5 ml.) and ether (20 ml.) were added to the residue, and the ether phase was removed, dried (Na_2SO_4) in the dark, and evaporated under a nitrogen atmosphere. The residual oil decomposed completely before crystallisation or sublimation could be effected.

(b) *With Adams catalyst in anhydrous methanol.* A suspension of Adams catalyst (*ca.* 10 mg.) in methanol (5 ml.) was saturated with hydrogen. 1,1′-Diphenylazoferrocene (0·197 g.), suspended in methanol (20 ml.), was added, and the mixture hydrogenated. Gas absorption was very slow and irregular. After 108 hr. the clear orange solution, presumably containing 1,1′-diphenylhydrazoferrocene was filtered by suction (with an immediate change in colour from orange to deep red) and evaporated to dryness (with an air leak), and the residual oil was passed in benzene down a column of alumina (30 × 3 cm.). A single pink-violet band yielded black crystals (0·0727 g.), m. p. 178—181° (from acetone), mixed m. p. with the starting material 180—182° (37% recovery).

Derivatives of 1,1′-Diaminoferrocene.—(a) *1,1′-Di(benzyloxycarbonylamino)ferrocene.* The crude oily diamine obtained by hydrogenation of 1,1′-diphenylazoferrocene (0·788 g., 0·002 mole) in acetic acid, was dissolved in pyridine (30 ml.), and the apparatus and solution purged with nitrogen during 12 min., while benzyloxycarbonyl chloride (2·73 g., 0·016 mole, 100% excess) was added. The pyridine was removed by distillation after 12 hr., and benzene (20 ml.), ethanol (5 ml.), and water (20 ml.) were added to the residue. The organic phase was washed with 2N-hydrochloric acid (6 × 50 ml.), dried, and evaporated. The residual oil, on chromatography on neutral alumina (20 × 2·5 cm.) in benzene, afforded yellow needles (0·022 g., crystallised from ether at −78°) of 1,1′-di(benzyloxycarbonylamino)ferrocene, m. p. 107—108° (lit.,[6] m. p. 107·5—108·5°).

(b) *1,1′-Di(ethoxycarbonylamino)ferrocene.* Crude 1,1′-diaminoferrocene (0·002 mole) was dissolved in tetrahydrofuran (10 ml.) and pyridine (5·5 ml.), and ethyl chloroformate (10 × 1 ml.) was added during 1·5 hr. The mixture was left under a nitrogen atmosphere for 5 hr., sodium hydrogen carbonate solution (20 ml.) added, and the benzene layer removed, neutralised, washed, dried, and evaporated. The residue was chromatographed in benzene on neutral alumina, the main yellow band yielding 1,1′-di(ethoxycarbonylamino)ferrocene (0·1 g., 14%), m. p. 118—120°. A single recrystallisation from methanol raised the m. p. to 121—123° (lit.,[6] m. p. 122—123°).

(c) *1,1′-Di(methoxycarbonylamino)ferrocene.* 1,1′-Diphenylazoferrocene (0·792 g.) was hydrogenated in acetic acid (7 ml.) as above, the solution evaporated, and the resultant mixture of the acetates of aniline and 1,1′-diaminoferrocene was treated in benzene with methyl chloroformate (4 × 1 ml. added at 10 min. intervals). After 5 hr., sodium hydrogen carbonate solution (20 ml.) was added, and the organic phase separated, washed, dried, and evaporated to a total volume of about 20 ml. This concentrate was placed on neutral alumina (35 × 2 cm.) and eluted with benzene. The first 750 ml. of eluate were evaporated, to yield a slightly yellow oil (0·54 g., 90%), b. p. 95° (bath)/0·05 mm., which solidified to white needles, m. p. 43°. Methyl carbanilate has m. p. 47°. The main yellow band was eluted with 1 : 1 chloroform–benzene (500 ml.) and evaporated to a yellow oil (0·4 g.) which crystallised from methanol as yellow-brown rods of *1,1′-di(methoxycarbonylamino)ferrocene* (0·33 g., 50%), m. p. 173—176°. Three recrystallisations from methanol yielded a sample of m. p. 177—178° (Found: C, 50·75; H, 5·0; N, 8·4. $C_{14}H_{16}FeN_2O_4$ requires C, 50·6; H, 5·0; N, 8·4%).

The authors thank the D.S.I.R. for a maintenance grant (to G. R. K.), and Dr. Schlögl for help.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, April 10th*, 1961.]

[10] Schlögl and Seiler, *Naturwiss.*, 1958, **45**, 337.

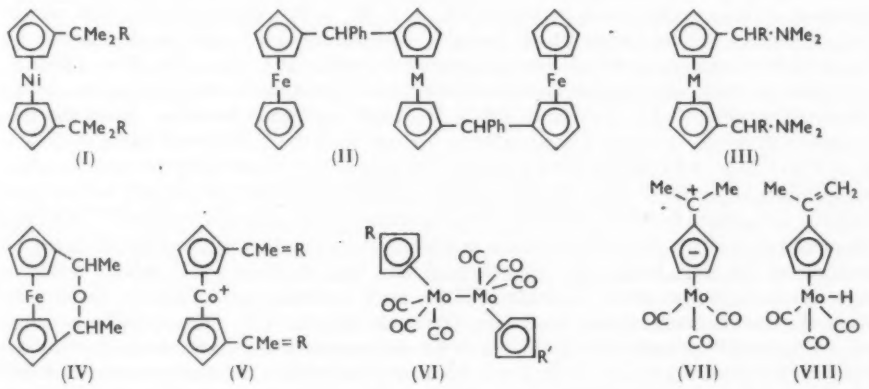
904. *Some Substituted Cyclopentadienyl Derivatives of Nickel, Cobalt, Iron, Molybdenum, and Titanium.*

By G. R. Knox, J. D. Munro, P. L. Pauson, G. H. Smith, and W. E. Watts.

The applicability to other transition metals of methods developed for the synthesis of ferrocenes is demonstrated. The extension of the fulvene synthesis to aminofulvenes is described.

In preceding papers methods have been described for the synthesis of substituted ferrocenes directly from substituted cyclopentadienes, in particular from fulvenes,[1] diazocyclopentadiene,[2] and the anions [3] of aminomethyl- and ethoxycarbonyl-cyclopentadienes. In the present paper we establish the applicability of these methods to those other transition metals which are known to afford stable cyclopentadienyl derivatives. This approach is particularly valuable for those compounds, *e.g.*, dicyclopentadienylcobalt(III) salts which cannot undergo electrophilic substitution. It should, however, be possible to modify substituents introduced by our direct method, and one example of such a reaction is included. Apart from the methylcyclopentadienyl and indenyl derivatives, the hydroxycyclopentadienides obtainable from cyclopentenones [4] and cyclopentadienones [5] are the only derivatives previously synthesised from these metals by such direct methods.

Fulvenes have previously been used by us in two ways: by addition to the $:CR_2$ group of alkyl or hydride ions to give alkylcyclopentadienide ions; and by proton abstraction to give alkenylcyclopentadienides. The former method has now been employed to obtain di(isopropylcyclopentadienyl)nickel (I; R = H) by reaction of dimethylfulvene and lithium aluminium hydride, and di-(αα-dimethylbenzylcyclopentadienyl)nickel (I; R = Ph) by reaction of dimethylfulvene and phenyl-lithium, followed in each case by treatment with tetrapyridinenickel chloride. We found the last reagent superior to nickel chloride or acetylacetonate for the preparation of dicyclopentadienylnickel. The product (I; R = Ph) was further converted by nitric oxide into nitrosyl-αα-dimethylbenzylcyclopentadienylnickel. The method has also been applied to ferrocenylfulvene, which with



[1] Knox and Pauson, *J.*, 1961, 4610.
[2] Knox and Pauson, *J.*, 1961, 4615.
[3] Osgerby and Pauson, *J.*, 1961, 4604.
[4] Benson and Lindsay, *J. Amer. Chem. Soc.*, 1957, **79**, 5471.
[5] Weiss and Hübel, *J. Inorg. Nuclear Chem.*, 1959, **11**, 42.

XUM

phenyl-lithium followed, respectively, by ferrous or cobaltous chloride afforded the trinuclear complexes (II; M = Fe or Co), the cobalt complex being isolated, after oxidation by air as the corresponding cobalt(III) perchlorate, picrate, or reineckate.

A further extension of the fulvene method was found in the use of α-dimethylaminofulvene, itself readily available by an improvement of Arnold and Zemlicka's method.[6] With lithium aluminium hydride followed by ferrous or cobaltous chloride this fulvene gave the diamines (III; R = H, M = Fe and Co), the latter being oxidised by air and isolated as the cobalticinium salt. The iron compound was shown to be identical with the known product.[3] Its homologue (III; R = Me, M = Fe) was obtained similarly by employing methyl-lithium in place of the hydride. The dimethiodide of this homologue is readily hydrolysed to the bridged ether (IV; two stereoisomers). This and other reactions of the amines (III; M = Fe) will be described in detail later.

The isopropenylcyclopentadienyl anion, derivable from dimethylfulvene and sodamide, was likewise employed to obtain a cobalt derivative (V; R = CH_2). The value of this approach is illustrated by the further transformation of this product into di(acetylcyclopentadienyl)cobalt(III) salts on ozonolysis. The stability of the parent dicyclopentadienylcobalt(III) ion to ozone had previously been demonstrated.[7]

A further use of fulvenes appeared possible in their direct reaction with metal carbonyls. Molybdenum carbonyl was the most promising of these submitted to preliminary trial with dimethylfulvene. The products of the same reaction have recently been reported in some detail by Abel *et al.*[8] and our own results are recorded only in so far as they differ from theirs. In 1,2-dimethoxyethane [8] or similar solvents the sole product from dimethylfulvene and molybdenum carbonyl is the " saturated " binuclear product (VI; R = R′ = Pr^i) whose formation must involve hydrogen abstraction from the solvent. Our initial experiments, however, were conducted in the absence of solvent (other than excess of fulvene) at 120°. The product obtained under these conditions gave eight bands on chromatography, all yielding crimson solids with very similar infrared spectra on elution. The first of these is due to the carbonyl (VI; R = R′ = Pr^i), identical with that product obtained under the conditions of Abel *et al.*[8] The second and largest single fraction was shown to be the unsymmetrical, monounsaturated product (VI; R = Pr^i, R′ = $CMe{:}CH_2$) by analysis, molecular-weight determination, and quantitative hydrogenation to the saturated product (VI; R = R′ = Pr^i). Although the other fractions have not been examined in detail, it appears reasonable to assume that the third is the diene (VI; R = R′ = $CMe{:}CH_2$), and that the later fractions are polymers derived from this and the above unsymmetrical product. The formation of these unsaturated derivatives may be compared with the formation of similar products from fulvenes by our sodamide method.[1] Although the mechanism of the present reaction is unknown, the formation of these products may be understood by considering the hypothetical first intermediate (VII) which would be expected to isomerise to the hydride (VIII). Such hydrides are known to decompose [9] below the reaction temperature used here, giving the dimers (VI). The hydridic hydrogen is not liberated [10] as molecular hydrogen in the presence of olefins, and in the present case just sufficient hydrogen is available from this source to produce the unsymmetrical product (VI; R = Pr^i, R′ = $CMe{:}CH_2$) or equimolecular amounts of the saturated and diunsaturated analogues.

In an extension of the fulvene method, diazocyclopentadiene was shown [2] to serve as a source of diarylazoferrocenes. This process has now been applied in preparations of 1,1′-diphenylazocobalticinium chloride and diphenylazocyclopentadienyltitanium dichloride.

[6] Arnold and Zemlicka, *Coll. Czech. Chem. Comm.*, 1960, **25**, 1302.
[7] Fischer, *Angew. Chem.*, 1955, **67**, 475.
[8] Abel, Singh, and Wilkinson, *J.*, 1960, 1321.
[9] Fischer, Hafner, and Stahl, *Z. anorg. Chem.*, 1955, **282**, 47.
[10] Sternberg and Wender, *Chem. Soc. Special Publ.*, 1959, No. 13, p. 35.

Experimental

For general directions see the preceding papers.

Improved Preparation of Dicyclopentadienylnickel.—A slurry of tetrapyridinenickel chloride (20 g., 0·045 mole) in tetrahydrofuran (40 ml.) was added to sodium cyclopentadienide [prepared from sodium wire (2·07 g., 0·09 g.-atom) and cyclopentadiene (6·6 g., 0·1 mole)] in tetrahydrofuran (100 ml.) under nitrogen. The mixture was stirred at room temperature for 30 min., then evaporated to dryness under reduced pressure. From the residue, the product (4·83 g., 57%) may be isolated by sublimation or by extraction with ligroin or ether, followed by rapid concentration and cooling to −70°; dicyclopentadienylnickel crystallises as green needles, m. p. 172—173° (decomp.) (Found: C, 63·5; H, 3·5. Calc. for $C_{10}H_{10}Ni$: C, 63·6; H, 5·3%). From larger runs yields up to 70% were obtained and isolation was conveniently effected by Soxhlet extraction.

1,1′-Di(isopropylcyclopentadienyl)nickel (I; R = H).—Dimethylfulvene (2·12 g., 0·02 mole) in ether (25 ml.) was added dropwise to a stirred suspension of lithium aluminium hydride (0·19 g., 0·02 mole) in ether (10 ml.) at room temperature, under nitrogen. A slurry of tetrapyridinenickel chloride (4·46 g., 0·01 mole) in tetrahydrofuran (40 ml.) was then added and the mixture stirred for 1 hr. Evaporation *in vacuo* left a brown gum which was chromatographed in ligroin on alumina (35 g.). This solvent eluted *1,1′-di(isopropylcyclopentadienyl)nickel* as a green, air-sensitive liquid (0·99 g., 35%), which was further purified by distillation at 128° (bath)/0·3 mm. (Found: C, 70·1; H, 8·2. $C_{16}H_{22}Ni$ requires C, 70·4; H, 8·1%).

1,1′-Bis-(αα-dimethylbenzylcyclopentadienyl)nickel (I; R = Ph).—Dimethylfulvene (2·12 g., 0·02 mole) in ether (10 ml.) was added dropwise with stirring and occasional cooling to phenyllithium [prepared from bromobenzene (3·5 g., 0·021 mole) and lithium (0·33 g., 0·05 g.-atom)] in ether under nitrogen. Tetrapyridinenickel chloride (4·46 g., 0·01 mole) in tetrahydrofuran (50 ml.) was then added and the mixture stirred at room temperature for 1 hr. Evaporation of the filtered mixture *in vacuo* gave a gum (2·87 g.) which was dissolved in ligroin. Concentration and cooling of the ligroin to −70° yielded green needles of *1,1′-di-(αα-dimethylbenzylcyclopentadienyl)nickel* (2·68 g., 63%), m. p. 109—110°, soluble in the common organic solvents (Found: C, 78·9; H, 7·3. $C_{28}H_{30}Ni$ requires C, 79·1; H, 7·1%).

Nitrosyl-(αα-dimethylbenzylcyclopentadienyl)nickel.—A ligroin solution (75 ml.) of the preceding product (2·12 g.) was saturated with nitric oxide, then filtered and evaporated *in vacuo*. The residue (0·81 g.) was chromatographed on alumina with ligroin as solvent. Distillation of the main band afforded *nitrosyl-(αα-dimethylbenzylcyclopentadienyl)nickel* (0·69 g., 51%) as a dark red liquid, b. p. 146°/0·3 mm. (Found: C, 61·7; H, 5·4; N, 5·0. $C_{14}H_{15}NNiO$ requires C, 61·8; H, 5·6; N, 5·2%).

1,1′-Di-(α-ferrocenylbenzyl)ferrocene (II; M = Fe).—Freshly prepared α-ferrocenylfulvene [3] (1·14 g.) in ether (25 ml.) was added dropwise to stirred phenyl-lithium [prepared in ether from bromobenzene (1·60 g., 0·01 mole) and lithium (0·2 g., 0·029 g.-atom)] under nitrogen. A pale yellow precipitate was formed almost instantly. After 1·5 hours' stirring, ferrous chloride [from ferric chloride (0·49 g., 0·003 mole)] in tetrahydrofuran (20 ml.) was added, and stirring continued for 66 hr. The mixture was poured into ice-water (200 ml.) and extracted with ether (3 × 50 ml.), and the combined extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The oily residue was chromatographed in ligroin–benzene (4 : 1) on alumina. Ligroin eluted starting material (0·061 g., 5·5%), and ligroin–benzene (4 : 1) then eluted *1,1′-di-(α-ferrocenylbenzyl)ferrocene* (II; M = Fe) (0·32 g., 21%) which crystallised from ligroin at 0° as a fine powdery yellow solid, m. p. 194—196° (Found: C, 72·5, 72·3, 72·2; H, 5·3, 5·7, 5·7. $C_{44}H_{38}Fe_3$ requires C, 72·0; H, 5·2%).

1,1′-Di-(α-ferrocenylbenzyl)cobalticenium Salts (II; M = Co^+).—The above experiment was repeated with anhydrous cobaltous chloride (0·65 g., 0·005 mole) in place of the ferrous salt. The reaction mixture was poured into ice and hydrochloric acid with free access of air. The resultant aqueous solution containing the 1,1′-di-(α-ferrocenylbenzyl)cobalticenium chloride was separated from the organic phase. The corresponding picrate, reineckate, and perchlorate were readily precipitated from this solution, but attempts to recrystallise these salts led to partial decomposition.

α-Dimethylaminofulvene.—Tetramethylformamidinium perchlorate [11] (10 g., 0·05 mole) was added in small portions to cyclopentadienylsodium [from ultrasonically dispersed sodium

[11] Arnold, *Coll. Czech. Chem. Comm.*, 1959, **24**, 760.

(1·4 g., 0·06 g.-atom) and an excess of cyclopentadiene] in tetrahydrofuran (180 ml.). After 12 hours' stirring, methanol (20 ml.) was added and the mixture poured into water (250 ml.) and extracted with ether. The dried (Na_2SO_4) extracts were evaporated under reduced pressure, leaving the crude fulvene (4·7 g., 78%) as a flaky yellow solid, m. p. 61—64°. Recrystallisation from ligroin raised this to m. p. 64—66° (lit.,[6] m. p. 50—64·5°) (Found: C, 79·2; H, 9·1; N, 11·7. Calc. for $C_8H_{11}N$: C, 79·3; H, 9·2; N, 11·6%).

1,1′-*Bis*-(1-*dimethylaminoethyl*)*ferrocene* (III; M = Fe, R = Me).—A solution of α-dimethylaminofulvene (1·6 g., 0·013 mole) in ether (20 ml.) was added dropwise to methyl-lithium [from lithium (0·28 g., 0·041 g.-atom) and methyl iodide (2·84 g., 0·02 mole)] in ether (40 ml.) under nitrogen. After 4 hours' stirring, anhydrous ferrous chloride [from ferric chloride (2·3 g., 0·014 mole)] in tetrahydrofuran (10 ml.) was added; the mixture began to reflux spontaneously and was stirred overnight. Methanol (10 ml.) was added and the whole then poured into water (200 ml.) and extracted with ether. The dried (Na_2SO_4) extracts were evaporated under reduced pressure and the viscous *product* (III; M = Fe, R = Me) (1·54 g., 71%) distilled at 120° (bath)/1 mm. (Found: C, 64·9; H, 8·3; N, 8·3. $C_{18}H_{28}FeN_2$ requires C, 65·8; H, 8·6; N, 8·5%). It forms an unstable dimethiodide.

1,1′-*Bis*(*dimethylaminomethyl*)*ferrocene* (III; M = Fe, R = H).—A solution of α-dimethylaminofulvene (1·21 g., 0·01 mole) in ether (10 ml.) was added dropwise to a sitrred suspension of lithium aluminium hydride (0·4 g., 0·01 mole) in ether (20 ml.) under nitrogen at room temperature. The mixture was stirred for 2 hr., then ferrous chloride [from ferric chloride (1·29 g., 0·008 mole)] in tetrahydrofuran (20 ml.) was added and stirring continued overnight. Ice was added, the ether layer was separated, the aqueous layer extracted with ether, and the combined ether solutions were dried (Na_2SO_4) and concentrated *in vacuo*. The residual amber oil (0·86 g., 58%) consisted of 1,1′-bis(dimethylaminomethyl)ferrocene (III; M = Fe, R = H), identical with the product previously described [3] as shown by its infrared spectrum and by the m. p.s and mixed m. p.s of the picrates and methiodides. It was further characterised by conversion of the dimethiodide with picric acid into the *dimethopicrate* which forms yellow needles from aqueous methanol, m. p. 228° (decomp.) (Found: C, 45·4; H, 4·4; N, 14·4. $C_{30}H_{34}FeN_8O_{14}$ requires C, 45·8; H, 4·4; N, 14·3%).

1,1′-*Bis*(*dimethylaminomethyl*)*cobalticenium Salts* (III; M = Co^+, R = H).—The preceding experiment was repeated with cobaltous chloride (1 g., 0·008 mole) in place of ferrous chloride. After addition of ice, the organic phase was extracted exhaustively with dilute hydrochloric acid in presence of air, and the combined aqueous solutions were brought to pH 4. The aqueous solution was divided into two portions, from which the reineckate and *tetraphenylborate* were severally precipitated (total yield 78%). The reineckate formed a red powder from methanol. The tetraphenylborate crystallised as a pale yellow powder from methanol (Found: C, 81·7; H, 7·2. $C_{64}H_{65}B_2CoN_2$ requires C, 81·5; H, 6·95%).

1,1′-*Di-isopropenylcobalticenium Salts* (V; R = CH_2).—Freshly distilled dimethylfulvene (21 g., 0·2 mole) was added to sodamide (from 4·6 g. of sodium) in liquid ammonia (200 ml.) under nitrogen. The mixture was stirred for 0·5 hr., and tetrahydrofuran (200 ml.) was then added as the ammonia evaporated. After brief warming to remove most of the residual ammonia, cobaltous chloride (13 g.) was added and stirring continued overnight. The product was poured on ice and hydrochloric acid and extracted with ether until the extracts became colourless. The yellowish-brown aqueous solution was then divided into several portions. From these, the 1,1′-di(isopropenylcyclopentadienyl)cobalt(III) compound was precipitated with picric acid as the *picrate*, crystallising from water as orange needles, m. p. 122·5—123° (Found: C, 53·4; H, 4·4. $C_{22}H_{20}CoN_3O_7$ requires C, 53·1; H, 4·1%), and with ammonium perchlorate as the *perchlorate*. The latter forms as an orange microcrystalline precipitate, sparingly soluble in water from which it may be recrystallised with addition of a little saturated aqueous ammonium perchlorate. A sample, further purified by slow precipitation from its acetone solution with ether, did not melt sharply, but gradually liquefied above 145° (Found: C, 52·5; H, 5·62. $C_{10}H_{13}ClCoO_4$ requires C, 52·1; H, 4·9%). The compound was also precipitated as tetraphenylborate (yellow powder, crystallisable by slow precipitation from acetone solution with water), reineckate (tan, acetone-soluble powder), tribromide (orange gum), and a tri(or poly?)iodide (dark brown, microcrystalline).

1,1′-*Diacetylcobalticinium Salts* (V; R = O).—A stream of ozone (0·005 g. per min.) was passed for 1 hr. through a solution of 1,1′-di-isopropenylcobalticenium perchlorate (1 g., 0·0027 mole) in chloroform (25 ml.) at 0°. Water (50 ml.) was then added and the mixture

heated on a steam bath for 1 hr. The mixture was distilled until all the chloroform was removed. From an aqueous extract of the chloroform distillate, formaldehyde (54 mg.) was precipitated as its dimedone derivative, m. p. and mixed m. p. 185—186°. The cooled aqueous distillation residue was divided into two equal portions. Addition of a saturated solution of Reinecke's salt to one of these precipitated *1,1′-diacetylcobalticenium reineckate* (0·52 g., 65%) crystallising from acetone as orange plates, m. p. 176—179° (with darkening from 155°) (Found: C, 36·4; H, 3·5; N, 14·0. $C_{18}H_{20}CoCrN_6O_2S_4$ requires C, 36·6; H, 3·4; N, 14·2%). The second portion gave a precipitate of the *tetraphenylborate*, which formed brown crystals (from acetone), m. p. 195—198° (decomp. from 165°) (Found: C, 77·2; H, 5·9. $C_{39}H_{34}BCoO_2$ requires C, 77·0; H, 5·8%). Both salts showed strong absorption at 1682 cm.$^{-1}$ (C=O) (KCl disc).

1,1′-Diphenylazocobalticenium Chloride.—Diazocyclopentadiene [2] (2·76 g., 0·03 mole) in ether (20 ml.) was added dropwise to a stirred solution of phenyl-lithium (0·03 mole) in ether (50 ml.) under nitrogen at −30°. A scarlet precipitate was formed. After 30 min. cobaltous chloride (1·94 g., 0·015 mole) was added and the mixture then stirred overnight, being allowed to warm gradually to room temperature. The solvent was removed *in vacuo*, 2N-hydrochloric acid (50 ml.) added, and the mixture heated to 100° for 10 min. The deep red solution was filtered hot and, on cooling, deposited *1,1′-diphenylazocobalticenium chloride* (71 mg.). Recrystallisation from 2N-hydrochloric acid gave dark red, slightly hygroscopic crystals, m. p. 138—139° (decomp.) (Found: C, 60·9; H, 4·1; N, 12·5; Cl, 7·9. $C_{22}H_{18}ClCoN_4$ requires C, 61·0; H, 4·2; N, 12·9; Cl, 8·2%). From half of the filtrate the corresponding *reineckate* (1·63 g.) was precipitated. Recrystallisation from acetone gave orange-brown crystals, m. p. 217—219° (decomp. from 190°) (Found: C, 43·2; H, 3·2; N, 19·3. $C_{26}H_{24}CoCrN_{10}S_4$ requires C, 43·6; H, 3·4; N, 19·6%). The remainder was precipitated as the *tetraphenylborate* (1·45 g.) which formed brown plates (from acetone), decomp. >160° (Found: C, 76·8; H, 5·1; N, 7·6. $C_{46}H_{39}BCoN_4$ requires C, 77·1; H, 5·4; N, 7·8%). The total yield of 1,1′-diphenylazocobalticenium salts was 30%.

Di(phenylazocyclopentadienyl)titanium Dichloride.—To phenylazocyclopentadienyl-lithium (0·03 mole), prepared as above, a solution of titanium tetrachloride (2·84 g., 0·015 mole) in tetrahydrofuran (20 ml.) was added and the mixture stirred at room temperature overnight. The solvent was removed *in vacuo*, the residue triturated with benzene, and the benzene extract evaporated again, to leave a red gum (2·8 g., 42·5%) which crystallised with some difficulty from benzene–ligroin. *Di(phenylazocyclopentadienyl)titanium dichloride* was obtained as a brown solid, m. p. 198—204° (decomp. from 175°) (Found: C, 57·2; H, 3·8; N, 11·9. $C_{22}H_{18}Cl_2N_4Ti$ requires C, 57·8; H, 4·0; N, 12·3%).

Hexacarbonyl(isopropenylcyclopentadienyl)(isopropylcyclopentadienyl)dimolybdenum (VI; R = Pr^i, R′ = CMe:CH$_2$).—Dimethylfulvene (17 g., 0·16 mole) and dimolybdenum hexacarbonyl (17 g., 0·07 mole) were heated under nitrogen at 120° for 8·5 hr. Starting materials were removed *in vacuo*, and the residue was chromatographed in light petroleum (b. p. 40—60°) on alumina, with the same solvent as eluent. The first band afforded hexacarbonyldi(isopropylcyclopentadienyl)dimolybdenum (VI; R = R′ = Pr^i) as purple-red crystals, m. p. 155—156° (lit.,[8] m. p. 163°), undepressed and identical in infrared spectrum with a sample prepared by the recorded method [8] [Found: C, 45·9; H, 3·95%; *M* (cryoscopic in benzene *), 520. Calc. for $C_{22}H_{22}Mo_2O_6$: C, 46·0; H, 3·9%; *M*, 574]. Elution of the second band afforded *hexacarbonyl(isopropenylcyclopentadienyl)(isopropylcyclopentadienyl)dimolybdenum* as purple crystals (from light petroleum), m. p. 119° [Found: C, 46·2; H, 3·6%; *M* (cf. above), 500. $C_{22}H_{20}Mo_2O_6$ requires C, 46·2; H, 3·5%; *M*, 572]. Six further bands separated on the column and were eluted with ligroin, benzene, and finally ether. All showed strong peaks in the metal–carbonyl region near 1957 and 1905 cm.$^{-1}$. They did not crystallise readily and the later fractions were undoubtedly polymeric. Three samples of the product (VI; R = Pr^i, R′ = CMe:CH$_2$) were hydrogenated at room temperature over 10% palladium-charcoal. In each case hydrogen uptake ceased after absorption of 1 molecule (±10%) [calculated after correction for a control value obtained similarly with the "saturated" product (VI; R = R′ = Pr^i$_2$)]. The hydrogenation product was identified by m. p., mixed m. p. and infrared comparison with the authentic product (VI; R = R′ = Pr^i).

We thank Dr. A. C. Syme and his staff for analytical data and molecular-weight determinations. We are indebted to the Ethyl Corporation for financial support which enabled

* Determined by an unpublished micro-method by A. C. Syme.

J. D. M. and G. H. S. to participate in this work. Part of the work (by P. L. P. and W. E. W.) was aided by the Air Force Office of Scientific Research of the Air Research and Development Command, U.S.A.F. We are also grateful to the D.S.I.R. for a maintenance grant (to G. R. K.) and to Esso Research Ltd., for supplies of cyclopentadiene.

THE ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY,
GLASGOW.

[*Received, April 10th*, 1961.

---

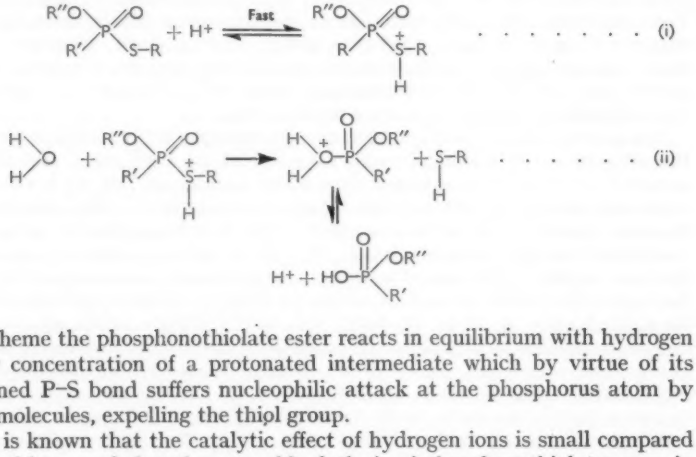
905. *The Concerted Action of Fluoride and Silver Ions on Diethyl Ethylphosphonothiolate in Aqueous Solution.*

By B. SAVILLE.

The hydrolysis of phosphonothiolate esters in neutral or acid solution, and the substitution reaction with fluoride ion, represented, $H_2O + RO{\cdot}PR(:O){\cdot}SR \longrightarrow HO{\cdot}PR(:O){\cdot}OR + RSH$, $F^- + RO{\cdot}PR(:O){\cdot}SR \longrightarrow F{\cdot}PR(:O){\cdot}OR + RS^-$, normally occur slowly. It is now shown that silver ions exert a powerful assistance in nucleophilic displacements of this type, high yields of ethyl ethylphosphonofluoridate being obtained, under mild conditions, in this way (second reaction).

Some kinetic measurements have been made concerning these assisted reactions for which mechanistic propositions are advanced.

THE hydrolysis in acid solution of phosphonothiolic esters $R''O{\cdot}PR'(:O){\cdot}SR$ has not been studied in detail, but if hydrogen-ion catalysis is assumed to operate, as is suggested by results on analogous reactions,[1,2] it appears that the probable reaction mechanism is:



According to this scheme the phosphonothiolate ester reacts in equilibrium with hydrogen ions to yield a low concentration of a protonated intermediate which by virtue of its considerably weakened P–S bond suffers nucleophilic attack at the phosphorus atom by the solvent (water) molecules, expelling the thiol group.

Qualitatively, it is known that the catalytic effect of hydrogen ions is small compared with that of hydroxyl ions, and that the rate of hydrolysis of phosphonothiolates even in strong mineral acid is so low that high temperatures are required to bring the reaction to a conveniently measurable rate. The low reactivity of the nucleophilic solvent towards phosphonothiolates, even in strongly acid solution, may reflect the very low degree of protonation of the sulphur atom in the sense of equation (i). This postulate seems plausible on the basis that sulphur is much less basic than oxygen towards hydrogen ions and other

[1] Hudson and Keay, *J.*, 1956, 3269.
[2] Ripper, 3rd Internat. Congr. Crop Protection, Paris, 1952. Reported in " Organic Insecticides," Metcalf, Interscience, New York, 1955.

highly positive centres, as indicated, for example, by the much higher dissociation constants of thiols than of the corresponding alcohols.

On the other hand, derivatives of bivalent sulphur can co-ordinate very powerfully with certain atomic centres, a phenomenon particularly well displayed in the case of mercuric and silver ions. A review [3] of ligand–acceptor affinities comments on the sequence $S \gg O$ for bonding with Ag^+. Accordingly, if the sulphur atom of a phosphonothiolate ester molecule were to co-ordinate with either mercuric or silver cations the P–S bond ought to be considerably weakened by interatomic repulsion so that the susceptibility of the phosphorus atom towards attack by nucleophiles would be enhanced. Thus the hydrolysis, alcoholysis, etc., of phosphonothiolates should be markedly catalysed by metal cations or other substances having a high affinity for sulphur.

The literature gives little information on such possible catalytic effects. Emmett and Jones,[4] however, when seeking a test to distinguish trimethyl phosphorothiolate $MeS{\cdot}P(O)(OMe)_2$ from the thiono-isomer $P(S)(OMe)_3$, found that aqueous or alcoholic silver nitrate gave with the former a precipitate having the approximate composition $(AgSMe)_2,AgNO_3$. This has been checked for triethyl phosphorothiolate, similar qualitative results being obtained. Since this reaction obviously indicates that silver ions assist nucleophilic attack on phosphorus and displacement of the thiol grouping by water, it was considered that the rate of attack by other nucleophilic reagents should be similarly enhanced.

The reaction between fluoride ions and diethyl ethylphosphonothiolate was used to test this prediction. Normally, this reaction in aqueous solution gives no phosphonothiolate decomposition during several days, but if silver ions were effective in assisting the displacement it would be a simple matter [5] to recognise the ethyl ethylphosphonofluoridate which would be formed thus: $F^- + EtO{\cdot}PEt(O){\cdot}SEt + Ag^+ \longrightarrow F{\cdot}PEt(O){\cdot}OEt + AgSEt$. Fluoride ion was chosen as the nucleophile to compete with water for the phosphonothiolate because it is known to possess a high reactivity towards reactive organophosphorus compounds, *e.g.*, phosphorochloridates,[6] and because the ion does not form a complex or a precipitate with silver ions in aqueous solution.

Experiment verified the predictions.

Experimental

Materials.—Inorganic materials were of " AnalaR " grade or of the best available purity. Diethyl ethylphosphonothiolate, prepared by Dr. B. C. Barrass (C.D.E.E., Porton), had b. p. 67—68°/2 mm., n_D^{25} 1·4725 (lit.,[7] b. p. 76·5°/4 mm., n_D^{20} 1·4730).

The reaction of mixed sodium fluoride–silver nitrate solution with diethyl ethylphosphonothiolate was performed in a fume cupboard, and apparatus was decontaminated with aqueous sodium hydroxide solution. Diethyl ethylphosphonothiolate (18·2 g., 0·1 mole) was added to sodium fluoride (6·3 g., 0·15 mole) in water (300 ml.), followed during 10 min. with stirring, by silver nitrate (25·5 g., 0·15 mole) in water (100 ml.). A white precipitate was deposited, and after a further 10 min. sodium chloride (10 g.) in water (50 (ml. was added to precipitate the excess of silver, the mixture was filtered under suction, and the precipitate was washed with water (100 ml.). The combined filtrate and washings were extracted with chloroform (3 × 50 ml.), and the extracts dried and distilled, affording crude *ethyl ethylphosphonofluoridate* (N.B.: extremely poisonous), b. p. 157—158°/760, 55—56°/11 mm. (11 g.), which, on redistillation, gave a pure ester, b. p. 24°/1·5 mm., n_D^{25} 1·3860 (Found: C, 34·9; H, 7·6; F, 13·4. $C_4H_{10}FO_2P$ requires C, 34·3; H, 7·2; F, 13·6%).

The precipitate was suspended in an excess of aqueous ammonia (to dissolve the halide), filtered off, and washed with dilute ammonia, water, and finally acetone before vacuum-drying to yield a silver ethyl sulphide nitrate (24 g.), m. p. 300° (Found: C, 7·7; H, 1·9; S, 9·2; Ag,

[3] Ahrland, Chatt, and Davies, *Quart. Rev.*, 1958, **12**, 265.
[4] Emmett and Jones, *J.*, 1911, **99**, 713.
[5] Marsh and Neale, *Chem. and Ind.*, 1955, 494.
[6] Dostrovsky and Halmann, *J.*, 1953, 508.
[7] Kabachnik and Mastryukova, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1953, 163; *Chem. Abs.*, 1954, **48**, 3244.

63·3. Calc. for $C_2H_5SAg,AgNO_3$: C, 7·1; H, 1·5; S, 9·5; Ag, 63·7%). It was insoluble in organic solvents, dilute nitric acid, and ammonia, but dissolved in an excess of sodium cyanide solution with the liberation of ethanethiol.

Hydrolysis of Diethyl Ethylphosphonothiolate in the Presence of Silver Ions.—The ester (0·1 mole) in water (100 ml.) was added to silver nitrate (0·2 mole) in water (200 ml.). A precipitate (25 g.), as above, was formed and after 20 min. sodium chloride (10 g.) in water (50 ml.) was added. The mixture was filtered and the precipitate washed with water before the filtrate and washings were made up to 1 l. with water. Titration with 0·1N-sodium hydroxide (phenolphthalein) indicated that 1·0 mole of diethyl ethylphosphonothiolate afforded 1·97 moles of acid, in accordance with the expectation that one mole of ethyl ethylphosphonic acid and one mole of nitric acid would be finally produced.

Kinetics of Decomposition of Diethyl Ethylphosphonothiolate in Aqueous Silver Nitrate–Sodium Fluoride Systems.—Appropriate volumes of concentrated stock solutions of sodium fluoride and silver nitrate were mixed, and they were diluted with water or sodium nitrate solutions whereby constant ionic strength was maintained. The mixtures, in flasks blackened to minimise photochemical action, were brought to the required temperature. Small volumes of concentrated aqueous diethyl ethylphosphonothiolate were added to give an initial ester concentration of about 0·001M. At convenient times aliquot parts (5 ml.) were withdrawn and added to N-potassium chloride (1 ml.) to precipitate the excess of silver, thereby stopping the reaction. The solutions were then filtered through Whatman No. 1 papers, and the filtrates (1 ml.) added to the dianisidine–peroxide reagent,[5] giving coloured solutions the intensities of which were independently found to be directly proportional to phosphonofluoridate concentration. Other experiments had shown that this colorimetric method suffers no interference from residual phosphonothiolate.

Another colorimetric procedure was also employed for the determination of residual phosphonothiolate in the filtrate. This does not suffer interference by phosphonofluoridate and was therefore suitable for following kinetically phosphonothiolate hydrolyses at the lower silver ion concentrations. To the filtrate (1 ml.) were added bromine water (1 ml.) (1 vol. of saturated aqueous bromine + 19 vol. of water), and after 1 min. 2% phenol–5% potassium bromide solution (1 ml.) in water; the whole was mixed, and pyridine–benzidine–cyanide reagent * added to a total volume of 10 ml. The intensity of the red colour developed after 15—20 min. was compared with that of a control, 1 cm. cells and Ilford 604 filters on a Hilger absorptiometer being used. There was a linear relation between phosphonothiolate concentration (0·00001—0·00012M) and absorptiometer readings. The method depends on the formation of ethanesulphonyl bromide [8] by the action of aqueous bromine on the phosphonothiolate, and the conversion of cyanide by the sulphonyl bromide [9] into cyanogen bromide which produces a red dye with pyridine and benzidine.

Treatment of Kinetic Data.—Suppose that in the presence of constant silver ion concentration the measured reactions may be represented:

$$\underset{(x)}{\mathrm{F{\cdot}PEt(:O){\cdot}OEt}} \xleftarrow[k_F]{F^-} \underset{(a-x-y)}{\mathrm{EtS{\cdot}PEt(:O){\cdot}SEt}} \xrightarrow[k_H]{H_2O} \underset{(y)}{\mathrm{HO{\cdot}PEt(:O){\cdot}OEt}} + H^+ + \mathrm{AgSEt}$$

Here, a is the initial phosphonothiolate concentration, x and y are the concentrations, at time t, of phosphonofluoridate and phosphonic acid formed in the reaction, and k_H and k_F are the first-order rate constants. The initial concentrations are always $(F^-) \gg a \ll (Ag^+)$.

It follows from the theory of competing first-order reactions that

$$y = xk_H/k_F. \qquad (1)$$

The rate of phosphonofluoridate formation is given by

$$dx/dt = k_F[\text{Phosphonothiolate}] = k_F(a - x - y). \qquad (2)$$

* This reagent is prepared by mixing 5 volumes of pyridine–hydrochloric acid (Aldridge, *Analyst*, 1945, **70**, 474) with 1 volume of 5% benzidine hydrochloride in 3% hydrochloric acid and 1 volume of 1% potassium cyanide. It may be used up to 2 hr. after being prepared.

[8] Stirling, *J.*, 1957, 3597.
[9] Saville, *Chem. and Ind.*, 1956, 660.

Substituting (1) in (2), one obtains

$$dx/dt = k_F[a - x(k_F + k_H)/k_F]$$

which rearranges to

$$dx/dt = (k_F + k_H)[ak_F/(k_F + k_H) - x]. \quad (3)$$

It may also be shown that on completion of the reaction the final value of x is $ak_F/(k_F + k_H)$, so that equation (3) becomes $dx/dt = (k_F + k_H)(x_\infty - x)$, which integrates to

$$\log_e [x_\infty/(x_\infty - x)] = (k_F + k_H)t.$$

Hence a plot of $\log_{10} (x_\infty - x)$ against t gives a straight line whose negative slope equals 1/2·303 of the sum of the rate constants k_F and k_H. (This treatment neglects aqueous hydrolysis of the phosphonofluoridate. This was studied and found to be a first-order process of *ca.* 8 hr. half-life, *i.e.*, very much slower than the processes being studied here.)

The variation of k_F with fluoride ion concentration can best be examined by plotting the values of $(k_F + k_H)$ (obtained in systems where silver ion concentration is kept constant and fluoride ion concentration varied) against the fluoride ion concentration. It was found in this way that k_F was directly proportional to fluoride ion concentration (Fig. 1), and for Table 1

TABLE 1.

Kinetic results for decomposition of diethyl ethylphosphonothiolate in aqueous silver nitrate–sodium fluoride solutions at 25°.

Phosphonothiolate initially ~0·001M. Total ionic strength 0·2, except where marked with asterisk.

	[Ag⁺] (10^{-2} g.-ion/l.)	[F⁻] (10^{-2} g.-ion/l.)	$k_H + k_F$ (min.$^{-1}$)	$k_F/[F^-] = k_2$ (l. mole^{-1} min.$^{-1}$)	
	5	0	0·0038 †	—	
	5	5	0·0405	0·734	0·729
	5	10	0·0762	0·724	
	10	0	0·0147 †	—	
	10	2	0·0418	1·36	
	10	4	0·0738	1·48	
	10	8	0·132	1·46	1·51
	10	10	0·165	1·50	
	10	12	0·191	1·47	
	10	19	0·304	1·52	
	20	0	0·056 †	—	
	20	5	0·264	4·16	4·04
	20	10	0·448	3·92	
	25	0	0·077 †		
	25	0·5	0·116	7·80	
	25	1	0·147	7·00	
*	25	2·5	0·268	7·56	7·58 *
	25	5	0·455	7·56	
	25	10	0·830	7·53	
	30	0	0·120 †		
	30	5	0·530	8·20	8·16
	30	10	0·932	8·12	
	40	0	0·191 †		
	40	10	1·38	11·9	11·9
	50	0	0·289 †		
	50	10	2·06	17·7	17·7

* No addition of $NaNO_3$, so that ionic strength was variable. † These values are k_H.

second-order constants (k_2) have been calculated by dividing k_F by the appropriate fluoride ion concentration. k_F values were obtained by subtracting k_H from $(k_F + k_H)$ after having independently determined k_H at various silver ion concentrations (Table 2).

TABLE 2.

Rates of hydrolysis of diethyl ethylphosphonothiolate in aqueous silver nitrate–sodium nitrate solutions at 25°. (The ionic strengths were varied by addition of sodium nitrate.)

$[Ag^+]$ (10^{-3} g.-ion/l.)	Ionic strength (M)	k_H (min.$^{-1}$)	$[Ag^+]$ (10^{-3} g.-ion/l.)	Ionic strength (M)	k_H (min.$^{-1}$)	$[Ag^+]$ (10^{-3} g.-ion/l.)	Ionic strength (M)	k_H (min.$^{-1}$)
5	0·200	0·0038*	20	0·500	0·0633	50	0·050	0·228
10	0·200	0·0146*	25	0·025	0·0600	50	0·200	0·289*
20	0·020	0·0414	30	0·200	0·120*	100	0·100	0·863
20	0·200	0·0560*	40	0·200	0·191*			

* Strictly comparable on an equal-ionic-strength basis.

DISCUSSION

The following facts emerge from the kinetic examination: (i) For the simple phosphonothiolate hydrolysis, the first-order rate constants, k_H, are fairly accurately proportional to the square of the silver ion concentration at constant ionic strength. (ii) The rates of ester substitution by fluoride ion are directly proportional to the concentration of fluoride

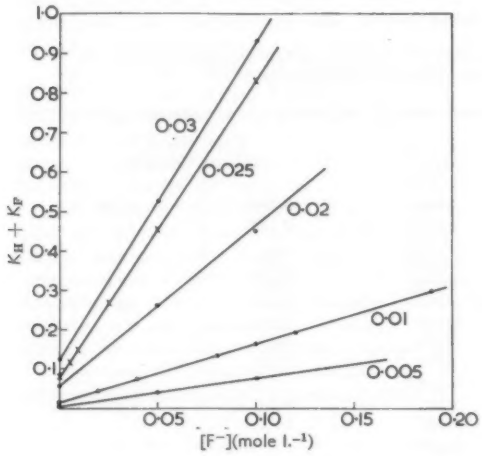
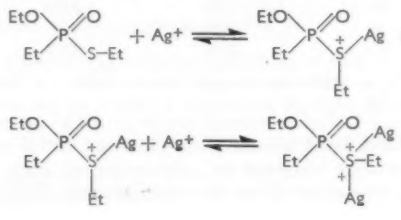


FIG. 1. Relation between first-order rate constants for diethyl ethylphosphonothiolate decomposition and fluoride ion concentration at various silver ion concentrations.

Silver concentrations (g.-ion l.$^{-1}$) are given against appropriate curve; ● ionic strength = 0·2; × ionic strength variable = 0·025 + $[F^-]$.

ion at a given $[Ag^+]$ (Fig. 1). (iii) The kinetic order with respect to silver ions for the fluoride ion substitution varies from near unity at low $[Ag^+]$ to a value approaching two at higher concentrations.

These results are accommodated if the ester is involved in stepwise co-ordination equilibria with silver ions, yielding small concentrations of the argentated intermediates (I) and (II) which are then susceptible to nucleophilic attack by solvent or fluoride ions:



$$(I) + H_2O \longrightarrow EtO{\cdot}PEt(:O){\cdot}OH + H^+ + AgSEt \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (v)$$

$$(I) + F^- \longrightarrow F{\cdot}PEt(:O){\cdot}OEt + AgSEt \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (vi)$$

$$(II) + H_2O \longrightarrow HO{\cdot}PEt(:O){\cdot}OEt + H^+ + Ag_2SEt^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (vii)$$

$$(II) + F^- \longrightarrow F{\cdot}PEt(:O){\cdot}OEt + Ag_2SEt^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (viii)$$

By assuming the equilibria (iii) and (iv) to be established rapidly and the displacements (vi) and (viii) to be relatively slow it is easy to show that the appropriate relation between k_2 and silver ion concentration takes the form

$$k_2 = \alpha[Ag^+] + \beta[Ag^+]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (ix)$$

where α and β are constants. This expression rearranges to $k_2/[Ag^+] = \alpha + \beta[Ag^+]$, so that a plot of $k_2/[Ag^+]$ against $[Ag^+]$ should be linear. Fig. 2 shows how the present results accord with this analysis. However, as seen already, the hydrolysis is of second order with respect to silver ions, making necessary the conclusion that the monoargentated intermediate (I) is not easily attacked by the moderately nucleophilic water molecules (reaction v) and that the main hydrolytic pathway (vii) occurs dominantly through the intermediate (II). This behaviour is rationalised by postulating that the potently nucleophilic fluoride ion is not especially discriminating with regard to the nature of the leaving groups $-\overset{+}{S}\!\!<^{Ag}_{Et}$, $-\overset{+}{S}\!\!<^{Ag}_{Et}$ of (I) and (II) and so attacks either intermediate, whereas the relatively feeble solvent nucleophiles find it necessary to seek out the intermediate (II) whose P–S bond is particularly weakened.

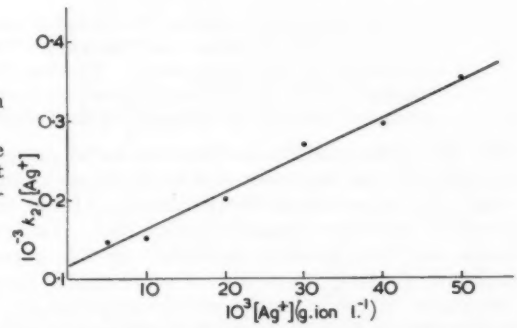


FIG. 2. Experimental test of equation (ix).

The implication from the positive $k_2/[Ag^+]$ intercept at zero $[Ag^+]$ is that fluoride ion can attack a monoargentated ester intermediate (I).

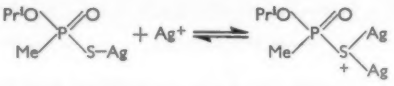
These arguments rest on the existence of equilibria (iii)—(iv). Now whereas (iii) may seem a plausible proposition by analogy with protonation equilibria in oxy-ester chemistry, a process such as (iv), whose existence seem necessary on the present interpretation, requires further comment. For example, the protonation counterpart, $-\overset{+}{O}\!\!<^{R}_{H} + H^+ \rightleftharpoons -\overset{+}{O}\!\!<^{H}_{R}$, has not been invoked to explain heterolytic phenomena in strong acids. However, there is evidence that more than one silver ion can co-ordinate with bivalent sulphur: silver ethyl sulphide, normally highly insoluble, dissolves appreciably in concentrated silver nitrate solution, perhaps by a reaction such as

$$EtSAg + Ag^+ \rightleftharpoons Et-\overset{+}{S}\!\!<^{Ag}_{Ag} \quad (III)$$

giving a soluble salt of the quasi-sulphonium ion (III).* Silver isopropyl methylphosphonothiolate is not appreciably decomposed in water, but it undergoes hydrolysis and

* It has also been found that many insoluble silver derivatives of primary thiols, suspended in tetrahydrofuran, dissolve easily on addition of concentrated aqueous silver perchlorate.

substitution with fluoride ion in the presence of an excess of silver ions. This behaviour seems to require the postulate that further Ag^+ co-ordination occurs, thus:



A simple argument against equilibrium (iv) is the electrostatic improbability of the double positive charge. This objection is removed if the Ag–S bond is covalent, in which case a more even charge distribution over the two atoms would lessen the positivity of the sulphur.

This work was performed during the tenure, at the Chemical Defence Experimental Establishment, Porton, Wilts., of a Civil Service Research Fellowship. The author thanks Dr. C. J. M. Stirling, of Queen's University, Belfast, for much stimulating discussion.

THE NATURAL RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48—56, TEWIN ROAD, WELWYN GARDEN CITY, HERTS. [*Received, April 20th*, 1961.]

---

906. *Spectrophotometric and Thermodynamic Properties of Some Copper and Iron Complexes.*

By B. R. JAMES, M. PARRIS, and R. J. P. WILLIAMS.

The absorption spectra of a number of cupric, cuprous, and ferrous complexes are described and discussed. The stabilities of some of the complexes are also determined. We show that description of the spectra requires a different relative emphasis on σ- and π-bonding in the complexes from that required in discussion of their stability.

THE absorption spectra of transition-metal complexes are relatively well understood. In particular the treatment of *d–d* transitions by ligand-field theory is in excellent agreement with experimental observations in so far as the number of bands and their relative positions are often accurately predictable.[1] Two problems remain, the intensity of the bands and their absolute positions. In this paper we describe an approach to these problems through the study of some cupric complexes. The other common optical transitions of the transition-metal complexes are the intense so-called charge-transfer bands. These transitions are less well understood. In the second part of the paper we examine the charge-transfer spectra of a large number of ferrous and cuprous complexes in an attempt to clarify the nature of these intense absorption bands. We have also examined the stabilities of a number of the complexes of these cations. A comparison between the spectroscopic and the thermodynamic information illustrates the very different effects of change of the ligand substituents on the different properties of the complexes.

Cupric Complexes.—Fig. 1 illustrates the absorption spectra of some typical cupric salts in pyridine. Table 1 lists the positions and intensities of the absorption bands of a series of such salts in the same solvent. The band shape varies little from compound to compound within a group. We shall follow ligand-field theory [1] in relating band positions to the field strength parameter, Δ, and the asymmetry of the bands to distortion from cubic symmetry (Fig. 1). A more detailed discussion follows below. The complexes can be formulated as (A) $Cu(py)_4(carboxylate)_2$, (B) $Cu(salicylaldehyde)_2(py)_2$, and (C) $Cu(salicylaldehyde\ imine)_2(py)_2$, where py = pyridine. The orders of the wavelengths, (C) < (A) < (B), show a decrease with increase in donor strength of the ligand, as expected,

[1] Orgel, "An Introduction to Transition-Metal Chemistry," Chapters 5 and 6, Methuen, London, 1960.

TABLE 1.

Spectra of cupric complexes in pyridine.

Anion	$\lambda_{max.}$ (mμ)	ε	Anion	$\lambda_{max.}$ (mμ)	ε	Anion	$\lambda_{max.}$ (mμ)	ε
Chloride	770	175	Salicylaldehyde:			Salicylaldehyde deriv.:		
Acetate	655	109	Unsubst.	725	91	Imine	585	75
Chloroacetate ...	665	126	3-NO_2	685	86	Methylimine	635	99
Stearate	650	99	5-NO_2	675	113	Ethylenedi-imine	605	257
Sebacate	650	84	3,5-$(NO_2)_2$	695	84	do. (5-Cl)	610s	317
			5-Cl	740	94	do. (3-MeO) ...	615s	291
Benzoate	650	111	5-Br	680	53	Imine (3-MeO) ...	600	90
Isonicotinate ...	655	111	3-Me	725b	110	do. (5-Cl)	590	100
Picolinate	660	88	5-Me	750vb	110			
Subst. benzoate:			3-MeO	785b	104			
o-NH_2	660 *	115	5-MeO	780vb	97			
m-NH_2	647 *	125	2-Hydroxy-1-naphthaldehyde ...	680	127			
p-NH_2	665 *	115						
o-NO_2	660	119						
m-NO_2	660	14						
p-NO_2	660	103						

* Shoulder at 25 mμ lower. b = broad; s = sharp; v = very.

and the relative sharpness of the peaks suggests that complexes of class (C) are almost regular octahedra (very sharp peaks), those of class (A) are tetragonal (one sharp peak with a broadening at longer wavelengths), and those of class (B) are most asymmetrical

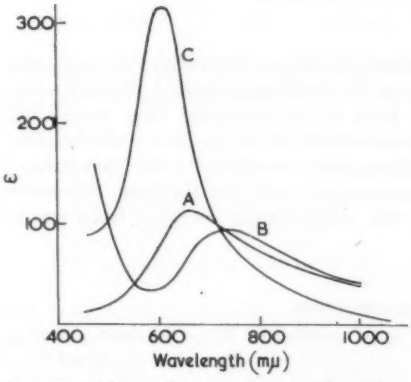


FIG. 1. Absorption spectra of the three groups of cupric complexes described in the text.

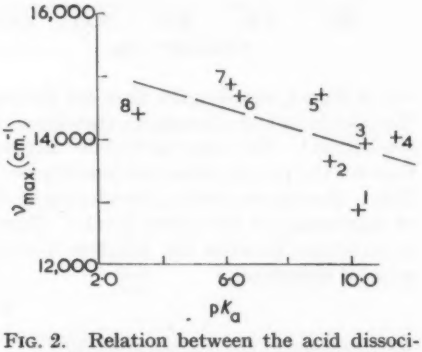


FIG. 2. Relation between the acid dissociation constants of a series of salicylaldehyde complexes and the frequency of the absorption maximum of their cupric complexes in pyridine.

1, 3-MeO^-. 2, 5-Cl^-. 3, Unsubst. 4, 3-Me. 5, 5-Br. 6, 3-NO_2. 7, 5-NO_2. 8, 3,5-$(NO_2)_2$.

(very broad peaks) (Table 1). We note that for the carboxylate complexes the position and intensity of the band change only slightly from ligand to ligand, although there are considerable changes in acid dissociation constants, pK_a. The latter can be used as a guide to σ-donor strength. In contrast, the spectra of the salicylaldehyde complexes are rather sensitive to the nature of substituents in the ligand. Fig. 2 is a plot of $\nu_{max.}$ for this series against pK_a of the ligand. It shows that the weaker bases give rise to the greater spectroscopic splitting factor, Δ. The weakest bases have nitro-substituents, which are strong π-acceptors; the strongest have methoxy- and methyl substituents, which are π-donors. We conclude that the spectra of these complexes are strongly dependent on π-bonding.

The stabilities of the complexes in dioxan–water [2] indicate a strong dependence of the stability constants of the salicylaldehyde complexes, β_n, on the acid dissociation constants of the ligands. The relation $\log \beta_2 = 0{\cdot}68pK_a + 1{\cdot}0$ is obeyed approximately. The dependence of stability on π-bonding is apparently much less than that of Δ, causing an opposing dependence of $\nu_{max.}$ and stabilities upon pK_a. For the benzoates the spectroscopic effects are less noticeable, presumably because the oxygen of a carboxylate ion is not as susceptible to π-bonding with the aromatic ring as is the oxygen of the phenoxide anion of salicylaldehyde. However, we note the absence of a dependence of $\lambda_{max.}$ upon pK_a even for the benzoates. For the salicylaldehyde di-imines methoxy-substituents again shift the absorption band to longer wavelengths although the pK_a values increase if such groups are present. A more remarkable effect is the relatively high extinction coefficients (250) of the chelated di-imines (derivatives of ethylenediamine), yet the peaks

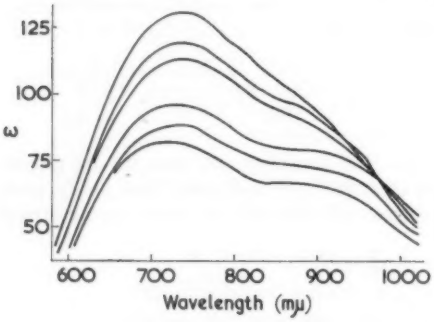


FIG. 3. Absorption spectra of some 2 : 1 complexes of cupric with 2,2′-bipyridyls in aqueous solution. Curves, reading downwards, are for: 5,5′-Et_2-4,4′-Me_2; 4,4′-Me_2; 4,4′-Et_2; 5,5′-Me_2; unsubst.; 4,4′-$(CO_2H)_2$.

are at longer wavelengths than for the non-chelated di-imines (derivatives of ammonia). We take both facts to suggest that the complexes of the chelated di-imines are very nearly octahedral.[1] The salicylaldehyde methylimine peak is at somewhat long wavelength than for the parent imine, presumably because there is some steric hindrance on chelation. This is also suggested by a broadening of the spectrum which could well arise from removal of degeneracy of the cupric levels. There is, however, no evidence for these differences in structure between the ethylenedi-imine and the methylimine complex from studies on solid complexes.[3]

TABLE 2.

Spectra of 2 : 1 cupric complexes.

1,10-Phenanthrolines (in H_2O).					2,2′-Bipyridyls (in 50% v/v dioxan–water)				
	Band I		Band II			Band I		Band II	
Ligand subst.	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε	Ligand subst.	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
None	710	56	920	45	None	720	86	940	75
5-Cl	700	50	940	39	5,5′-Me_2	730	88	920	80
5-NO_2	700	44	950	32	4,4′-Et_2	745	170	~900	~100
5-Me	720	64	905	55	4,4′-Me_2	735	101	920	90
5-Ph	730	69	910	61	5,5′-Et_2-4,4′-Me_2	740	112	920	100
5,6-Me_2	725	78	900	67	5,5′-$(CO_2H)_2$	695	83	950	70
3,5,6,8-Me_4	725	81	885	70	4,4′-Ph_2	710	103	950	> 80
4,7-Me_2	740	96	880	70	5,5′-$(CO_2Et)_2$	710	70	?	?
					4,4′-$(CO_2Et)_2$	700	50	?	?

Table 2 gives the band positions and intensities of some cupric 2,2′-bipyridyl(bipy) and 1,10-phenanthroline(phenan) complexes (cf. Fig. 3). The stability of these complexes is approximately proportional to pK_a.[4] As pointed out there must be considerable π-bond

[2] Jones, Poole, Tomkinson, and Williams, *J.*, 1958, 2001.
[3] Meuthen and von Stackelberg, *Z. anorg. Chem.*, 1960, **305**, 279.
[4] James and Williams, *J.*, 1961, 2007.

stabilisation in these complexes.[1,2,5] There is also very considerable steric hindrance between the first and the second 1,10-phenanthroline ligand as the difference log K_1 — log $K_2 \simeq 4{\cdot}0$ is much greater than the usual difference between the step constants of the cupric ion with chelating ligands, *e.g.*, for ethylenediamine log K_1 — log $K_2 \simeq 1{\cdot}0$. Now the different bands of a particular $Cu^{II}(phenan)_2$ or $Cu^{II}(bipy)_2$ complex are usually sufficiently separated for us to allocate bands to transitions (Figs. 3 and 5). We then observe that, whereas band I (750 mμ) (see Fig. 3) shows little dependence of $\lambda_{max.}$ upon ligand substituent, its intensity (or the total area under both bands) increases markedly as pK_a increases [4] (Fig. 4). The position of band II (900 mμ) moves to shorter wavelengths

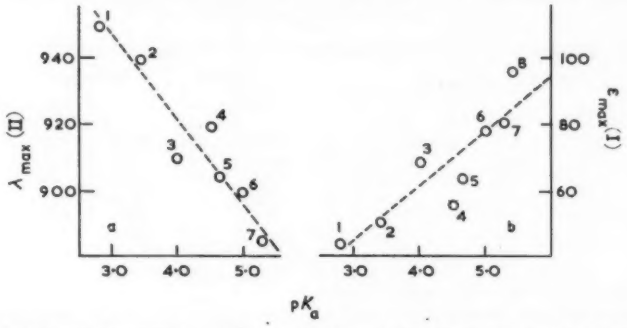


FIG. 4. Relations between $\lambda_{max.}$ (II) and pK_a and between ε (I) and pK_a for a series of 2 : 1 cupric complexes with 1,10-phenanthrolines. 1, 5-NO_2; 2, 5-Cl; 3, 5-Ph; 4, unsubst.; 5, 5-Me; 6, 5,6-Me_2; 7, 3,5,6,8-Me_4.

with increasing pK_a while band I moves to slightly longer wavelengths. As the substituents are far from the co-ordination centre and the tetragonal element in the complexes

TABLE 3.

Step stability constants.

1,10-Phenanthroline derivative	log K_1	log K_2	og K_3
Unsubst.	8·80	6·64	4·94
2-Methyl	7·40	6·40	V. small
2,9-Dimethyl	~6·10	~5·60	V. small

must be increasing in the sequence of basicity we reject any suggestion that a shift toward octahedral symmetry occurs with change of substituent to higher basicity. We suggest instead that the shift of peak I to longer wavelengths is due to the reduction of π-bonding to which transition I will be expected to be sensitive, $d_{zy} \longrightarrow d_{x^2-y^2}$. The shift to shorter wavelengths of peak II is due to increase in σ-bonding, for this transition should be but very little sensitive to π-bonding, $d_{xy} \longrightarrow d_{x^2-y^2}$. The series of observations is common to 1,10-phenanthrolines and bipyridyls. Here, as in the benzoates, salicylaldehydes, salicylaldehydedi-imines, and acetylacetonates,[2] the lack of simple correlations between the positions of ligand field bands and their stabilities does not permit us to use the simple electrostatic model to calculate from absorption spectra contributions to complex stability from *d*-level splitting. As this procedure is not permissible in these simple series it appears most improbable that it can be legitimate in the discussion [1] of the relative stabilities of complexes MX in comparison with MY where X and Y differ more grossly, *e.g.*, where X is water and Y ammonia. The above observations confirm [6] too that when an electron spin resonance spectrum of the cupric ion is to be analysed it will prove to be more valuable

[5] Williams, *Discuss. Faraday Soc.*, 1958, **26**, 123.
[6] Maki and McGarvey, *J. Chem. Phys.*, 1958, **29**, 31, 35.

to determine σ-bonding from the value of $g_{||}$ than from $g_{\perp}$ which is liable to be very sensitive to π-bonding.

Gross steric hindrance to planar binding of two phenanthroline molecules can be introduced by substituents in the 2-position. The cupric complexes should be driven from octahedral toward tetrahedral symmetry with distortion in both cases as steric hindrance increases. The electron energy levels of the cupric ion should become inverted as the change in symmetry takes place [1] (Fig. 5). We expect then that the more intense band will be at the longer wavelength in tetrahedral (distorted) complexes. The spectra of the complexes are shown in Fig. 6, where this prediction is born out. There is also a considerable increase in intensity, so that the transition probability is increased about three

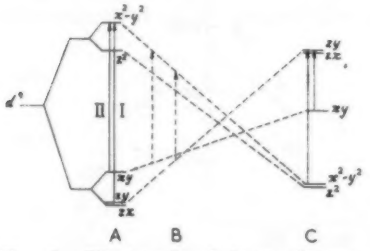


FIG. 5. Electron levels in cupric complexes indicating the transitions I and II which are resolved in the 2,2′-bipyridyl complexes (Fig. 3), and the effect of change of field symmetry from octahedral with tetragonal distortion (A) to tetrahedral with distortion (C). B is an intermediate case.

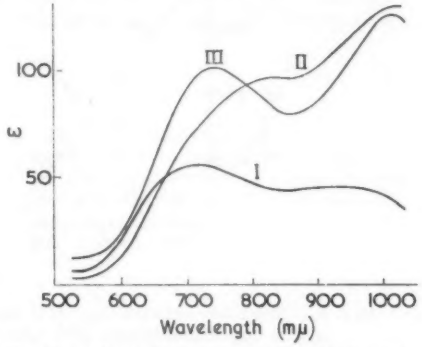


FIG. 6. Absorption spectra of the 2 : 1 cupric complexes with (I) 1,10-phenanthroline, and (II) 2-methyl- and (III) 2,9-dimethyl-1,10-phenanthroline.

times on going to the tetrahedral complex. This change is expected as a tetrahedron lacks a centre of inversion. There is a gradual change in the spectrum from the phenanthroline to the 2,9-dimethyl-1,10-phenanthroline by way of the 2-methylphenanthroline complex. There is, moreover, a remarkable change in the step stability constants,[4] as shown in Table 3.

The stability data suggest that the co-ordination around the cupric ion changes from octahedral to tetrahedral on addition of the first ligand, which is consistent with the spectroscopic observations. In this series of complexes the wavelengths of the transitions are not very different in the octahedral and tetrahedral complexes. Theory would predict an ~50% reduction of field strength on change to the lower co-ordination. Possibly the unexpected size of the field strength in the tetrahedral complexes arises from reduction of the Cu–N distances owing to the greatly reduced steric hindrance between ligands in the complexes of lower co-ordination number.

A spectrum of interest is that of the 4,7-dihydroxy-1,10-phenanthroline–cupric complex. Maximum absorption is at 460—470 mμ and the extinction coefficient is ~1250. The wavelength of the *d–d* transition is shorter and the extinction coefficient greater than in any other known cupric complex, raising the problem whether *d–d* transitions may be dissociated from charge-transfer transitions in extreme cases. We shall treat this problem in another paper.

We have also measured the spectra of the cupric complexes of $Ph{\cdot}As(CH_2{\cdot}CO_2^-)_2$ and $S(CH_2{\cdot}CO_2^-)_2$: neither of these ligands has a very marked effect on the position of the *d–d* band of the cupric ion relative to its position in water, whereas both increase the intensity of the bands considerably. As in previous papers we take the intensity changes to reflect changes in covalency, although there is no evidence for this type of change from

Δ values. The stability constants for the ligand $S(CH_2 \cdot CO_2^-)_2$ with several cations follow the Irving–Williams stability series.[7] These complexes provide another example of the persistence of this stability order even when Δ in the complexes is not markedly different from the value in water.[5]

Charge-transfer Spectra.—We have drawn attention earlier[8] to the similarity in absorption spectra between the spectra of $Cu^I(phenan)_2$ and $Fe^{II}(phenan)_3$ spectra. We have now made a large number of additional measurements which are summarised in Table 4. There is still a general linear correlation between $\lambda_{max.}(Cu^I)$ and $\lambda_{max.}(Fe^{II})$, but it is not as exact as was found for the more limited range. Incidentally we note that the $\lambda_{max.}$

TABLE 4.

Absorption spectra of some cuprous and ferrous complexes.

	Cuprous		Ferrous			Curpous		Ferrous	
2,2′-Bipyridyl subst.	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε	2,2′-Bipyridyl subst.	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
None	434	5270	523	9200	4,4′-$(CO_2Et)_2$	483	7130	545	14,000
5,5′-Et_2-4,4-Me_2 ...	430	5530	525	10,700	5,5′-$(CO_2Et)_2$	496	4150	~570	~2000
4,4′-Me_2	430	5700	530	9900	5,5′-$(CO_2Me)_2$	492	?	No colour?	
4,4′-Et_2	437	6150	530	10,600	4,4′-$(CO_2^-)_2$	457	7600	538	11,100
6,6′-Me_2	455	6460	—	—	4,4′-$(CO_2H)_2$	482	8300	547	11,000
4,4′-$(Ph \cdot CH_2 \cdot CH_2)_2$	433	6180	532	11,000	5,5′-$(CO_2^-)_2$	455	~4000	562	5500
5,5′-Me_2	436	6800	512	9520	5,5′-$(CO_2H)_2$	475	?	—	—
4,4′-Ph_2	463	10,300	550	21,700	3,3′-$(CO_2^-)_2$ ... 3,3′-$(CO_2H)_2$ ...	U.V.		U.V.	

Measurements refer to 50% v/v dioxan–water solutions, except for the Fe^{II} complex with diethyl 2,2′-bipyridyl-5,5′-dicarboxylate which was investigated in 75% dioxan–water.

values for the charge-transfer bands of Cu^I–O_2 (600 mμ) in hæmocyanin and of Fe^{II}–O_2 (900 mμ) in hæmoglobin as well as of Cu^I–S^- (300 mμ) in the cuprous and Fe^{II}–S (400 mμ) in the ferrous salt of cysteine lie near the same line. In charge-transfer spectra there appears to be a correlation between Fe^{II} (low spin) and Cu^I spectra extending over some 400 mμ. We are now seeking similar correlations with other reducing cations, *e.g.*, low-spin chromous and vanadous.

During the measurements on the ferrous–bipyridyl complexes we found that the maximum intensity of the spectrum of the diethyl 2,2′-bipyridyl-5,5′-dicarboxylate complex (FeP) was very low. We therefore investigated the stability and spectra of the step complexes of this ligand in some detail. The three step stability constants were obtained by the method of corresponding solutions: they are given in Table 5 with, for comparison, those of the ferrous–1,10-phenanthroline complex.

TABLE 5.

Stability constants of ferrous–diethyl 2,2′-bipyridyl-5,5′-dicarboxylate and, in parentheses, ferrous–1,10-phenanthroline.

	$\log \beta_n$ *	$\lambda_{max.}$	ε
FeP_1	2·5 (5·9)	520 (450)	100 (~1,000)
FeP_2	4·5 (?)	545 (?)	300 (?)
FeP_3	6·5 (2·15)	570 (510)	2,000 (11,000)

* Probable error ±0·30.

We conclude that, unlike the tris-1,10-phenanthroline complex, the complex FeP_3 is not a low-spin complex, but is an equilibrium mixture of the two spin forms containing a large proportion of the high-spin ion. At room temperature there is not more than 20% of the low-spin form. This has been confirmed by direct measurement of the magnetic moments in solution, which will be reported in a later paper. The proportion of the two

[7] Irving and Petit, unpublished work.
[8] Williams, *J.*, 1955, 137.

forms is strongly dependent on temperature, as judged by changes of absorption spectra. We also find the tris-4,4′-dicarboxylate complex to be virtually wholly in the low-spin form. This ligand has a higher basicity (pK_a 2·45) than the 5,5′-compound (pK_a 0·85), but the two ligands have very similar absorption spectra with the cupric ion, *i.e.*, the values of Δ are similar. We therefore suggest that the low-spin–high-spin equilibrium is not controlled so much by the value of Δ, the spectroscopic splitting parameter [determined from the study of the spectra of high-spin (*e.g.*, cupric) complexes] as by changes in π-bonding. The 5,5′-dicarboxylate ligand is a relatively poor π-acceptor, as the substituent groups are *meta* to the nitrogen, whereas the 4,4′-groups are *para* and are strong π-acceptors. Now we have already shown that the *d–d* transitions of the cupric ion are very sensitive to π-bonding between the ligand and the cation. We conclude that the high-spin–low-spin equilibrium is even more sensitive to π-bonding. This is not so surprising when it is remembered that the low-spin state is merely a very highly excited *d*-state configuration relative to the high-spin state.

Experimental.—Materials. Preparation of the substituted salicylaldehydes has been described.[3] The benzoic acids were commercially available. The substituted bipyridyls

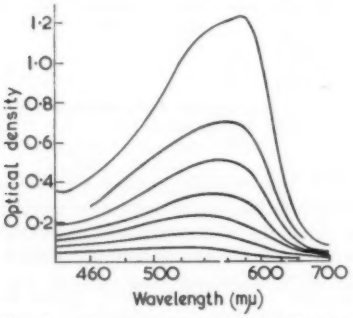


FIG. 7. Ferrous complex with diethyl 2,2′-bipyridyl-5,5′-dicarboxylate. $[Fe^{II}] = 2 \times 10^{-3}$M. Ligand concns. are $2·0 \times 10^{-3}$M for the lowest and $16·0 \times 10^{-3}$M for the top curve, with $2·0 \times 10^{-3}$M intervals. The solvent is 75% dioxan–water and 0·1N-sulphuric acid.

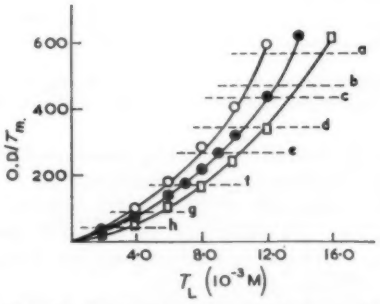


FIG. 8. Corresponding solutions, positions of equal optical density (O.D.)/T_M, at different T_L, and three ferrous concentrations, *viz.*: ○, $0·5 \times 10^{-3}$M; ●, $1·0 \times 10^{-3}$M; □, $2·0 \times 10^{-3}$M. Other conditions as for Fig. 7.

were given to us by Professor G. M. Badger (Adelaide University, Australia). The substituted phenanthrolines have been described elsewhere.[4] The procedure used for determination of the stability constants of the copper complexes has been published.[2,4] The stability constants for the stepwise formation of the ferrous complex of diethyl 2,2′-bipyridyl-5,5′-dicarboxylate were obtained by the method described below. Absorption spectra were measured on a Unicam S.P. 600, a Beckman DU, or the recording Beckman spectrophotometer. The degrees of complex formation in the solutions were known from the measurements of the stability constants.

Diethyl 2,2′-bipyridyl-5,5′-dicarboxylate complexes. The absorption spectra of 0·002M-solutions of ferrous sulphate and ligand, at the various strengths indicated, and all in 0·1N-sulphuric acid and 3 : 1 dioxan–water, appear in Fig. 7. The procedure of corresponding solutions[9] is to vary both T_M (total ferrous) and T_L (total ligand), giving solutions of equal optical density at a chosen wavelength. Our measurements at 540 mμ are plotted in Fig. 8. From this graph, plots of T_M against T_L (Fig. 9A) for equal optical density (see broken lines on Fig. 8) are obtained. The slope of the lines gives $\bar{n}$, the degree of formation, and the intercept

[9] Fronaeus, *Acta Chem. Scand.*, 1951, **5**, 139.

XUM

on T_L ($T_M = 0$) gives [L] (the concentration of free ligand). The formation function of pL against $\bar{n}$ so obtained is given in Fig. 9B. By curve-fitting methods the values of K_1, K_2, and K_3 were derived. The method of corresponding solutions is open to considerable error, as is recognised in the quoted constants. Extinction coefficients were then calculated.

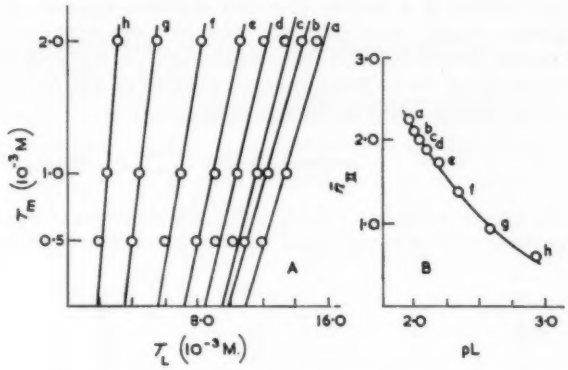


FIG. 9. (A) Plots of T_L against T_M at equal optical density (see Fig. 8). (B) The resulting plot of $\bar{n}$ against −log [free ligand].

We thank Professor G. M. Badger for gifts of chemicals, the Wellcome Trust and The Royal Society for the loan of spectrophotometers, the D.S.I.R. for a research grant (to B. R. J.), and The British Rubber Producers' Research Associates for a research grant (to M. P.).

THE UNIVERSITY, OXFORD. [*Received, May 8th*, 1961.]

---

907. *The Mechanism and Steric Course of Octahedral Aquation. Part IV.*[1] *The Aquation of* cis- *and* trans-*Dichloro- and* cis- *and* trans-*Chlorohydroxo-bis(ethylenediamine)cobalt*(III) *Salts.*

By M. E. BALDWIN, S. C. CHAN, and M. L. TOBE.

The rate constants of the solvolytic aquation of the *cis*- and *trans*-[Co en$_2$Cl$_2$]$^+$ and *cis*- and *trans*-[Co en$_2$OHCl]$^+$ cations have been determined over a range of temperature and the Arrhenius parameters calculated. The products of these reactions, [Co en$_2$H$_2$OCl]$^{2+}$ and [Co en$_2$OH,H$_2$O]$^{2+}$, isomerise to equilibrium mixtures at rates comparable with those of their formation. The rates of isomerisation and the positions of equilibrium are reported. When corrections are made for the isomerisation of the product, it is found that *trans*-[Co en$_2$Cl$_2$]$^+$ and *trans*-[Co en$_2$OHCl]$^+$ yield 35% and 75%, respectively, of the *cis*-aquo-product directly, whereas both the *cis*-isomers yield only *cis*-product.

THE dependence of the rates of aquation of complex ions of the type [Co en$_2$ACl]$^{n+}$ (where en = ethylenediamine) on the nature of the non-participating ligand A, has led to the postulation of two mechanisms for the process, a unimolecular (S_N1) mechanism when A = OH, Cl, N_3, or NCS, and a bimolecular (S_N2) mechanism when A = OH_2, NH_3, or NO_2.[2,3] Previous investigations of the steric course of aquation of the *trans*-isomers showed that the bimolecular aquations (A = NH_3 [4] or NO_2 [2]) lead to no steric change, whereas two unimolecular aquations (A = N_3 [1] or NCS [5]), result in considerable steric

[1] Part III, Staples and Tobe, *J.*, 1960, 4803.
[2] Asperger and Ingold, *J.*, 1956, 2862.
[3] Basolo and Pearson, "Mechanism of Inorganic Reactions," John Wiley and Sons, Inc., New York, 1958, p. 166.
[4] Tobe, *J.*, 1959, 3776.
[5] Baldwin and Tobe, *J.*, 1960, 4275.

change. The work presented in this paper shows that in the other two cases where unimolecular aquation is expected (A = OH or Cl) the *trans*-isomer yields a considerable amount of *cis*-aquo-product.

(1) *The Isomerisation of* cis- *and* trans-*Aquochlorobis(ethylenediamine)cobalt*(III) *Salts.*—The colour of a freshly prepared acidified aqueous solution of *trans*-[Co $en_2H_2OCl]Cl_2$ slowly changes from green to violet at room temperature although the amount of free chloride ions in solution does not change. A study of the changes that take place in the spectrum of an acidified aqueous solution of the *trans*-isomer showed (Fig. 1) that the colour change is due to the isomerisation,

$$cis\text{-}[Co\ en_2ClH_2O]^{2+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} trans\text{-}[Co\ en_2H_2OCl]^{2+}$$

The specific rate constant, $(k_1 + k_{-1})$, for approach to equilibrium was determined spectrophotometrically by following the change of optical density at 520 mμ where there was a

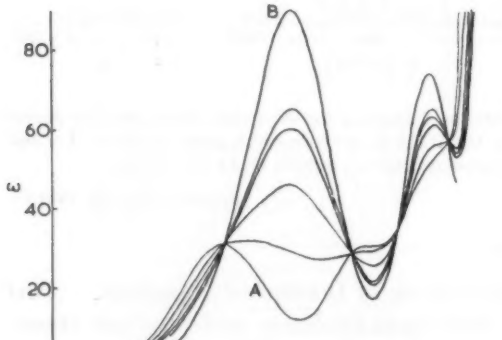


FIG. 1. Change in the spectrum of an acidified solution of *trans*-[Co $en_2OHCl]Cl,H_2O$.

A = *trans*-[Co $en_2H_2OCl]^{2+}$.
B = *cis*-[Co $en_2H_2OCl]SO_4$.

Intermediate curves, read upwards from A, are for 60, 143, 301 and 395 min., respectively, at 25°.

maximum difference between the extinction coefficients of the two isomers. The change obeyed a first-order rate law, the rate constant being obtained from the slope of the semi-logarithmic plot of $\log_{10}(D_\infty - D_t)$ against time, where D_∞ was the optical density determined after ten half-lives. Provided that the solution was sufficiently acidic (0·01N-nitric acid), the subsequent replacement of co-ordinated chlorine did not interfere. The results are collected in Table 1 where it will be seen that the values obtained for $(k_1 + k_{-1})$ at 25° are the same whether equilibrium is approached from the *trans*- or the *cis*-side. Since equilibrium lies closer to the *cis*-side most of the data are derived from solutions originally containing the *trans*-isomer. The position of equilibrium does not change significantly between 0° and 40°, indicating that the activation energies of the *trans* to *cis*, and the *cis* to *trans*, change must be similar.

(2) *Isomerisation of* cis- *and* trans-*Hydroxoaquobis(ethylenediamine)cobalt*(III) *Cations.*—Kruse and Taube [6] recently studied the relation between the isomerisation and the water exchange of these isomers. Anticipating difficulties due to the acid–base relationship between the diaquo-, hydroxoaquo-, and dihydroxo-cations they studied the isomerisation of a self-buffered mixture of the diaquo- and hydroxoaquo-complexes where the major path of isomerisation was through the latter. The results are in very good agreement with this work when corrections are made for the difference in temperature.

We have found that the anticipated difficulties do not arise and that the solvolytic

[6] Kruse and Taube, *J. Amer. Chem. Soc.*, 1961, **83**, 1280.

disturbance due to dissolving the appropriate hydroxoaquo-complex in carbon dioxide-free water affects the rates of isomerisation less than the experimental error does. Although it is possible to measure the rate of isomerisation by studying the light-absorption

TABLE 1.

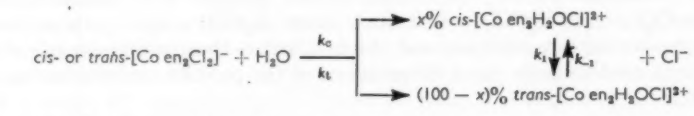
Isomerisation of the aquochlorobis(ethylenediamine)cobalt(III) cations in aqueous nitric acid (0·01N).

The *trans*-isomer was supplied as *trans*-[Co en$_2$OHCl]Cl,H$_2$O which was converted instantly into the aquo-complex on dissolving in acid. The *cis*-isomer was supplied as *cis*-[Co en$_2$H$_2$OCl]SO$_4$,1·5H$_2$O.

Temp.	Initial config.	Initial [Complex] (mmole/l.)	$(k_1 + k_{-1})$ $\times 10^4$ (sec.$^{-1}$)	*cis*-Isomer (%) at equil.	Temp.	Initial config.	Initial [Complex] (mmole/l.)	$(k_1 + k_{-1})$ $\times 10^4$ (sec.$^{-1}$)	*cis*-Isomer (%) at equil.
0·0°	*trans*	4·02	0·0162	73	35·0°	*trans*	4·04	4·4	74
,,	,,	5·08	0·0161	74	,,	,,	5·08	4·4	74
,,	,,	6·00	0·0161	73	,,	,,	6·07	4·3	74
,,	,,	7·04	0·0158	73	,,	,,	6·92	4·3	74
25·0	,,	4·00	0·97	73	40·1	,,	4·04	8·7	73
,,	,,	4·95	0·96	73	,,	,,	5·12	8·7	73
,,	,,	6·01	0·97	73	,,	,,	6·04	8·7	73
,,	,,	6·97	0·96	73	,,	,,	6·99	8·8	73
,,	*cis*	4·10	0·94	73					
,,	,,	5·04	0·95	74					
,,	,,	6·07	0·95	73					
,,	,,	7·06	0·96	73					

changes of a solution of the hydroxoaquo-complex, it was found more convenient to take, and then acidify, samples of the reaction mixture, converting the labile hydroxoaquo-species into the relatively inert diaquo-species, which could then be examined spectrophotometrically. The specific rate constants for the approach to equilibrium $(k_1 + k_{-1})$ were determined in the usual way from the change in optical density of the acidified samples measured at 490 mμ and are given in Table 2, together with the isomeric composition at equilibrium. The value obtained by direct measurement (59% of *cis*) is in very good agreement with that calculated by Bjerrum and Rasmussen [7] from the equilibrium data for the diaquo-, hydroxoaquo-, and dihydroxo-bis(ethylenediamine)cobalt(III) cations (58·6% of *cis*).

(3) *The Steric Course of Aquation of* cis- *and* trans-*Dichlorobis(ethylenediamine)cobalt*(III) *Salts.*—



The kinetics of these reactions have been thoroughly examined in the past and are repeated here only as far as is necessary to elucidate the steric course of the processes. The rates of aquation at 25° determined titrimetrically in 0·01N-nitric acid agree with those published by Mathieu [8] and Basolo *et al.*[9] The steric course of aquation of the *cis*-dichloro-complex has been determined by Mathieu [10] who studied the mutarotation of the optically active complex and showed that the product, when first formed, had the same specific molecular rotation as an independently resolved, specimen of *cis*-[Co en$_2$H$_2$OCl]$^{2+}$. The spectrophotometric analysis described below confirms that no *trans*-product is initially formed.

The rate constant for the isomerisation of the product is about three times that for aquation of the *trans*-dichloro-isomer and about one-half of that of the *cis*. In neither case

[7] Bjerrum and Rasmussen, *Acta Chem. Scand.*, 1952, **6**, 1265.
[8] Mathieu, *Bull. Soc. chim. France*, 1936, **3**, (*a*) 2121, (*b*) 2152.
[9] Basolo, Boston, and Pearson, *J. Amer. Chem. Soc.*, 1953, **75**, 3089.
[10] Mathieu, *Bull. Soc. chim. France*, 1937, **4**, 687.

can the steric course be determined by analysing the solution when the aquation is complete since the composition will be controlled by the isomerisation equilibrium. However, by measuring the composition of the product at various stages of the reaction it was not difficult to correct for the isomerisation. In both cases, the composition of the product,

TABLE 2.

Isomerisation of *trans*-aquohydroxobis(ethylenediamine)cobalt(III) perchlorate in aqueous solution.

Temperature = 0·0°			Temperature = 10·2°		
Initial [Complex] (mmole/l.)	$(k_1 + k_{-1})$ $\times 10^5$ (sec.$^{-1}$)	*cis* (%) at equil.	Initial [Complex] (mmole/l.)	$(k_1 + k_{-1})$ $\times 10^5$ (sec.$^{-1}$)	*cis* (%) at equil.
6·07	6·6	59	6·03	42	59
6·08 *	6·6	59	7·02	42	59
7·05	6·6	59	8·08	42	59
8·00	6·6	59	9·07	42	59
9·08	6·6	59			

* Starting with *cis*-[Co en$_2$OH,H$_2$O]Br$_2$,H$_2$O.

expressed as % of *cis*-product, was plotted against % of reaction completed, and the extrapolation of these curves back to zero reaction gave the composition of the product as formed by aquation. These data are plotted in Fig. 2, where the extrapolations are guided by functions of the correct form.[11]

A complete spectrophotometric analysis of the three components of the reaction mixture was not possible in either case since the spectra of the *trans*-dichloro- and *trans*-aquochloro-cations are too similar, as are the spectra of the *cis*-dichloro- and *cis*-aquochloro-cations. The problem was solved by a combined spectrophotometric and titrimetric technique. Two samples were withdrawn from the reaction mixture within a short time of one another and frozen. The ionic chloride content of the first sample was determined by titration and the optical density of the second sample was determined at an appropriate wavelength. The chloride titre afforded the total amount of aquo-complex present, and the apparent molar extinction coefficient the concentration of one of the two aquochloro-isomers. When the *trans*-dichloro-isomer was studied the optical density was measured at 490 mμ where the extinction coefficients of the *trans*-dichloro- and *trans*-chloroaquo-cations are equal (14·1) and very different from that of the *cis*-chloroaquo-cation (72·2). When the *cis*-dichloro-isomer was studied optical densities were measured at 525 mμ where $\varepsilon(cis\text{-}Cl_2) = \varepsilon(cis\text{-}H_2OCl) = 89{\cdot}2$, and $\varepsilon(trans\text{-}H_2OCl) = 13{\cdot}2$. These results were used to determine the rate constants and also to calculate the quantities required for Fig. 2. The constants used to guide the extrapolations of the product composition back to zero reaction were:

$$k_e = 2{\cdot}44 \times 10^{-4}\ \text{sec.}^{-1};\ k_t = 3{\cdot}53 \times 10^{-5}\ \text{sec.}^{-1};$$
$$k_1 + k_{-1} = 9{\cdot}57 \times 10^{-5}\ \text{sec.}^{-1};\ \text{and}\ k_1/k_{-1} = 0{\cdot}36.$$

Measurements were made at 25·0°.

It will be seen from Fig. 2 that

$$trans\text{-}[Co\ en_2Cl_2]^+ + H_2O \longrightarrow \left.\begin{matrix}35\%\ cis\\65\%\ trans\end{matrix}\right\}[Co\ en_2H_2OCl]^{2+} + Cl^-$$

and

$$cis\text{-}[Co\ en_2Cl_2]^+ + H_2O \longrightarrow 100\%\ cis\text{-}[Co\ en_2H_2OCl]^{2+} + Cl^-$$

(4) *The Aquation of* cis- *and* trans-*Chlorohydroxobis(ethylenediamine)cobalt*(III) *Salts.*—

$$cis\text{- or }trans\text{-}[Co\ en_2OHCl]^- + H_2O \xrightarrow[k_t]{k_e} \begin{cases} x\%\ cis\text{-}[Co\ en_2OH,H_2O]^{2+} \\ k_1 \rightleftharpoons k_{-1} \\ (100-x)\%\ trans\text{-}[Co\ en_2OH,H_2O]^{2+} \end{cases} + Cl^-$$

[11] Ingold, Nyholm, and Tobe, *J.*, 1956, 1691.

(4a) *Kinetics.* The rates of aquation of both these isomers have been determined at 25° by Basolo *et al.*[12] who studied the rate of release of co-ordinated chloride from a mixture of both isomers together with some *trans*-dichloro- and *cis*- and *trans*-dihydroxo-complex. The rate constants quoted agree well with those found in this work with pure complexes. We followed the progress of the reaction by titrating the ionic chloride released or by measuring the change in the conductivity. Both our methods gave similar rate constants and, at the higher temperatures where the reaction is too fast for accurate sampling, only the conductivity method was used. Attempts to prepare a pure sample of *cis*-[Co en_2OHCl]Br were unsuccessful and the product was always contaminated with up to 50% of *cis*-Co en_2OH,H_2O]Br; recrystallisation only served to increase the amount of the latter salt.

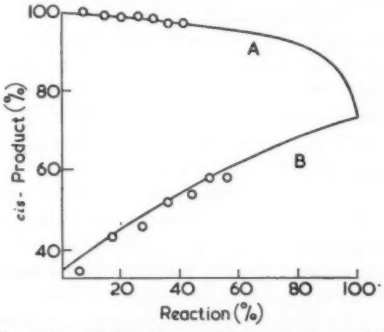


FIG. 2. Product analyses during the aquation of (A) *cis*- and (B) *trans*-[Co en_2Cl_2]Cl at 25·0°.

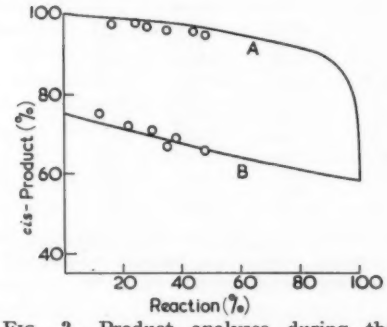


FIG. 3. Product analyses during the aquation of (A) *cis*- and (B) *trans*-[Co en_2OHCl]$^+$ at 0°.

Although the impure complex could be used to determine the rate of aquation it was useless for determination of the steric course and so the *cis*-chlorohydroxo-complex was prepared *in situ* by adding about 4% less than the calculated amount of alkali to a solution of *cis*-[Co en_2H_2OCl]SO_4. The titrimetric rate constants were determined from the semi-logarithmic plots of $\log_{10}(V_\infty - V_t)$ against time, where V_t and V_∞ are the titres of silver nitrate at time t and after ten half-lives respectively. The experimental " infinity " corresponds almost exactly to the titre expected if the remaining aquochloro-complex did not aquate under the experimental conditions. The conductimetric rate constants were computed from the conductivity data in an analogous way. The rate constants, determined over a range of temperature, are given in Table 3. Values obtained by other workers are included for comparison.

(4b) *Steric course.* Owing to the rapid isomerisation of the products, it was necessary, once again, to analyse the reaction mixture during the reaction and apply corrections for the isomerisation. The samples were acidified before measurement so that the labile hydroxo-complexes were converted into the relatively inert aquo-complexes. The relation between the spectra of the chloroaquo- and the diaquo-complex is very similar to that between the dichloro- and the chloroaquo-species, so that a complete spectrophotometric analysis was not feasible. By combining chloride analyses with optical-density measurements it was possible to calculate " % of reaction " and " % of *cis*-product." The *cis*-chloroaquo-complex was studied at 496 mμ where the molar extinction coefficients of the *cis*-chloroaquo-, the *cis*-diaquo-, and the *trans*-diaquo-complex are 77·0, 77·0, and 18·7, respectively; and the *trans*-chloroaquo-complex was studied at 470 mμ where the molar extinction coefficients of the *trans*-chloroaquo-, the *cis*-diaquo-, and the *trans*-diaquo-complex are 23·3, 65·2, and 24·1, respectively. The values derived from results obtained

[12] Basolo, Meeker, and Pearson, *J. Amer. Chem. Soc.*, 1956, **78**, 2673.

TABLE 3.

First-order rate constants for the aquation of *cis*- and *trans*-chlorohydroxobis-(ethylenediamine)cobalt(III) salts in aqueous solution.

Temp.	Initial [Aquo-complex] (mmole/l.)	Added [Alkali] (mmole/l.)	10^4k (sec.$^{-1}$)	Method *
		cis-[Co en$_2$OHCl]$^+$		
0·0°	7·38	7·00	3·12	T
,,	8·42	8·00	3·13	T
,,	9·37	9·00	3·13	T
,,	10·41	10·00	3·14	T
,,	7·18	6·80	2·97	C
,,	8·24	8·00	3·01	C
,,	9·31	9·00	3·00	C
,,	10·38	10·00	3·02	C
10·2	7·44	7·00	15·9	T
,,	8·49	8·00	15·8	T
,,	9·39	9·00	15·7	T
,,	10·44	10·00	15·8	T
23·75	7·41	7·00	98	C
,,	8·50	8·00	100	C
,,	9·38	9·00	102	C
,,	10·43	10·00	101	C

Temp.	Initial [Complex] (mmole/l.)	10^4k (sec.$^{-1}$)	Method *
	trans-[Co en$_2$OHCl]$^+$		
0·0°	4·50	0·315	T
18·8	3·42	5·64	C
25·0	3·72	16·5	C
,,	6·20	15·9	T
31·6	12·6	43·5	C

* T = titrimetric; C = conductimetric.

Basolo, Meeker, and Pearson [12] report the values $1·3 \times 10^{-2}$ and $1·4 \times 10^{-3}$ sec.$^{-1}$ for the *cis*- and the *trans*-isomer, respectively, at 25°.

from neutral solutions at 0° are plotted in Fig. 3. The extrapolations were guided by the appropriate functions, with the following values:

$$k_c = 3·07 \times 10^{-4} \text{ sec.}^{-1}; \quad k_t = 3·14 \times 10^{-5} \text{ sec.}^{-1};$$
$$k_1 + k_{-1} = 6·59 \times 10^{-5} \text{ sec.}^{-1}; \text{ and } k_1/k_{-1} = 0·698.$$

It was found that

$$\textit{trans}\text{-[Co en}_2\text{OHCl]}^+ + \text{H}_2\text{O} \longrightarrow \left.\begin{matrix}75\%\ \textit{cis}\text{-} \\ 25\%\ \textit{trans}\text{-}\end{matrix}\right\}\text{[Co en}_2\text{OH,H}_2\text{O]}^{2+} + \text{Cl}^-$$

$$\textit{cis}\text{-[Co en}_2\text{OHCl]}^+ + \text{H}_2\text{O} \longrightarrow 100\%\ \textit{cis}\text{-[Co en}_2\text{OH,H}_2\text{O]}^{2+} + \text{Cl}^-$$

(5) *Summary and Discussion.*—The results reported above are collected in Table 4.

TABLE 4.

Rates, Arrhenius parameters and products of the aquation of dichloro- and chlorohydroxo-bis(ethylenediamine)cobalt(III) complexes in aqueous solution

$$k = B \exp(-E/\boldsymbol{R}T)$$

Group A	k at 25° (sec.$^{-1}$)	E (kcal./mole)	$\log_{10} B$	*cis*-Product (%)
(*a*) *cis*- or *trans*-[Co en$_2$ACl]$^+$ + H$_2$O ⟶ *cis*- and *trans*-Co en$_2$AH$_2$O]$^{2+}$ + Cl$^-$				
cis-Cl	$2·44 \times 10^{-4}$	22·2 [35]	12·5	100
trans-Cl	$3·53 \times 10^{-5}$	24·2 [35]	13·0	35
cis-OH	$1·2 \times 10^{-2}$ *	23·1	15·0	100
trans-OH	$1·6 \times 10^{-3}$	26·2	16·4	75
(*b*) *cis*-[Co en$_2$AH$_2$O]$^{2+}$ $\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}$ *trans*-[Co en$_2$AH$_2$O]$^{2+}$				
Cl	$9·5 \times 10^{-5}$	27·2	15·9	73 (equil.)
OH	$5·0 \times 10^{-3}$ *	28·1	18·2	59 ,,

* Extrapolated values.

In a previous publication,[13] the relation between the polar effects of the non-participating ligands, the mechanism of the aquation reaction, and the orientation of the substitution was discussed. In those aquations to which a unimolecular mechanism has been assigned there is always a path whereby a suitably placed lone pair of electrons on a non-participating ligand can conjugate with the metal and assist the dissociation of the leaving group. The stereochemical requirement of this electromeric effect is that the two conjugating orbitals be non-orthogonal, a situation which can only be achieved without alteration of the bond angles of the remaining ligands when the two groups are *cis*. A ligand *trans* to the dissociating group cannot develop the electromeric effect without some change in geometry, with a result that the entry of water into the " cobaltium ion " intermediate may lead to a product whose configuration differs from that of the starting compound.

These conclusions are supported by experimental fact, since all the *cis*-isomers studied are aquated with complete retention of configuration, whereas every *trans*-$[Co\ en_2AX]^{n+}$ complex to which a unimolecular mechanism for aquation has been assigned on other grounds is aquated with extensive change of configuration. Although the concept of a positive electromeric ($+E$) effect assisting the unimolecular dissociation predicts steric change when a *trans*-isomer reacts, it does not allow an estimate to be made of its extent.

For the *trans*-complexes of the type $[Co\ en_2ACl]^{n+}$ the labilising effect (and possibly the $+E$ effect) of ligand A decreases along the series $OH > N_3 > Cl > NCS$, whereas the amounts of steric change observed are 75%, 20%,[1] 35%, and >50%,[5] respectively. There appears to be no correlation between the labilising effect and the amount of steric change, nor should this be expected since it should be realised that, once the relative positions of the five remaining ligands are changed in forming the " cobaltium ion," the product composition will be determined by the factors controlling the subsequent entry of water. With the limited amount of experimental evidence available it is premature to attempt an explanation of this aspect of the reaction and we are now studying the effects of other electron-displacing groups and of other dissociating ligands in an attempt to throw more light on the subject.

There is also a lack of correlation between the rates of aquation and the activation energies for the *trans*-isomers of the above series. The values found are 26·2, 23·1,[1] 24·2,[8b] and 30·4 [11] kcal./mole for the ligands A = OH, N_3, Cl, and NCS, respectively, arranged in order of decreasing labilising power. This does not vitiate the idea that the labilising power of ligand A arises from its electron-displacement properties. To understand this it is necessary to consider the solvation of the complex ion, especially the difference in the solvation of the complex and the transition state. Since all the reactions under comparison involve stretching of the Co–Cl bond in complex ions of the same charge and similar size, most of the contributions to the solvent effect will be constant along the series and can be neglected. Any specific solvation about ligand A that is disturbed by an increase in the A–Co–en bond angle will produce an effect—probably one of desolvation —that will depend very much upon the nature of A. In the absence of a satisfactory model it is not possible to make accurate calculations of this effect but, since the interaction is probably hydrogen-bonding in character, the desolvation on formation of the transition state may be approximated to a melting process, and the relative enthalpy and entropy changes can then be deduced from those of the melting of ice. The free-energy change for the fusion of ice is, of course, zero at 0° and can be estimated to be very small (<0·2 kcal./mole) at 25°,[14] so that the free energy of desolvation will only contribute a fraction of the rate. The entropy and enthalpy changes for the fusion of ice, however, are quite considerable, ~3·6 cal. $mole^{-1}$ $deg.^{-1}$ and ~1·6 kcal./mole, respectively.[14] It can be concluded that, although the partial desolvation resulting from the change in geometry will have a marked effect on the energy and entropy of activation, the effects will work

[13] Ingold, Nyholm, and Tobe, *Nature*, 1960, **187**, 477.
[14] Cf. Dorsey, " Properties of Ordinary Water Substance," Reinhold Publ. Corp., New York, 1940, pp. 264, 480.

XUM

in opposition to one another and have little effect on the rate of aquation at temperatures not greatly removed from 0°.

Experimental

Preparations.—*trans*-Dichlorobis(ethylenediamine)cobalt(III) chloride was prepared by the standard method [15] and recrystallised from the minimum amount of water at 35° {Found: Co, 20·6; Cl^-, 12·4; co-ordinated Cl, 24·8. Calc. for $[Co(C_2H_8N_2)_2Cl_2]Cl$: Co, 20·7; Cl^-, 12·4; co-ordinated Cl, 24·9%}.

cis-Dichlorobis(ethylenediamine)cobalt(III) chloride was prepared from the *trans*-isomer [15] and recrystallised from water at 35° {Found: Co, 19·4; Cl^-, 11·7; co-ord. Cl, 23·4. Calc. for $[Co(C_2H_8N_2)_2Cl_2]Cl,H_2O$: Co, 19·4; Cl^-, 11·7; co-ord. Cl, 23·4%}.

cis-Chloroaquobis(ethylenediamine)cobalt(III) sulphate was prepared from *trans*-[Co en_2Cl_2]Cl by Werner's method.[16] It was recrystallised by dissolving it in the minimum amount of water at 40° (5 g. in 100 ml.), cooling the filtered solution in ice, and adding ethanol (50 ml.) {Found: Co, 16·7; co-ord. Cl, 10·0; Cl^- absent. Calc. for $[Co(C_2H_8N_2)_2H_2OCl]SO_4,1\frac{1}{2}H_2O$: Co, 16·6; co-ord. Cl, 10·0%}.

trans-Hydroxochlorobis(ethylenediamine)cobalt(III) chloride was made by the method of Meisenheimer and Kinderlen [17] by adding an aqueous solution of diethylamine to *trans*-[Co en_2Cl_2]Cl. The dove-grey paste that was formed was filtered off, washed successively with 7 : 3 ethanol–water, ethanol, and ether. The crude product was dissolved in ice-cold water (6·5 g. in 25 ml.), and the solution filtered as quickly as possible. Ethanol (26 ml.) was added and the mixture cooled in ice. The crystals formed were filtered off, washed with alcohol and ether, and dried in a stream of air. At least one more recrystallisation was necessary to give a pure product {Found: Co, 20·65; Cl^-, 12·60; co-ord. Cl, 12·4. Calc. for $[Co(C_2H_8N_2)_2OHCl]Cl,H_2O$: Co, 20·65; Cl^-, 12·45; co-ord. Cl, 12·45%}.

cis-Hydroxoaquobis(ethylenediamine)cobalt(III) bromide was prepared by Werner's method [18] from [Co en_2CO_3]Br and recrystallised on addition of alcohol and ether to a concentrated aqueous solution {Found: Co, 15·0; Br, 40·8. Calc. for $[Co(C_2H_8N_2)_2OHH_2O]Br_2,H_2O$: Co, 15·0; Br, 40·8%}. In 0·1N-perchloric acid it has a spectrum identical with that published for the *cis*-diaquo-complex.[7]

trans-Hydroxoaquobis(ethylenediamine)cobalt(III) perchlorate was prepared from *trans*-[Co en_2Cl_2]NO_3. The latter complex (15 g.) was suspended in water (30 ml.), and this mixture heated. Some of the complex dissolved and was aquated but most remained undissolved. The solution was decanted and passed through a column of anion-exchange resin (Amberlite IR-A 400; OH^- form) and washed out with a further 40 ml. of water. The combined effluent, which contained only [Co $en_2(OH)_2$]OH was allowed to react with the unchanged *trans*-dichloronitrate and then recycled through the resin. This process was repeated until all the solid had dissolved. The effluent was acidified to pH 3 with 72% perchloric acid and then freeze-dried to a volume of 40 ml. Pyridine (3 ml.) was then added drop by drop to the solution cooled in ice. A crystalline precipitate of the trans-*hydroxoaquo-perchlorate* separated and was filtered off, washed very carefully with alcohol and ether, and dried over concentrated sulphuric acid (yield, 3·6 g.) {Found: equiv., 210. $[Co(C_2H_8N_2)_2(OH)H_2O](ClO_4)_2,\frac{1}{2}H_2O$ requires equiv. $= \frac{1}{2}M = 210$}. A solution of this complex in 0·1N-perchloric acid has a spectrum identical with that published for the *trans*-diaquo-complex.[7]

[The equivalent weight was determined by passing a solution of a known amount of the complex through a cation-exchange resin column (Amberlite IR 120; H^+ form) and titrating the perchloric acid in the effluent with standard alkali.]

Kinetics.—The reaction solutions were made up by dissolving a weighed amount of the complex in the solvent previously brought to the temperature of the reaction. For the titrimetric and spectrophotometric investigations samples were withdrawn from the reaction mixture from time to time by means of a pipette surrounded with an ice-filled jacket. The reaction was stopped, either by cooling the sample to −78° or by adding it to acid. The ionic chloride was determined by passing the sample through a cation-exchange resin (Amberlite IR 120; H^+ form) and estimating the hydrochloric acid in the effluent by Volhard's method. Since

[15] Bailar, *Inorg. Synth.*, 1946, **2**, 222.
[16] Werner, *Annalen*, 1912, **386**, 122.
[17] Meisenheimer and Kinderlen, *Annalen*, 1924, **438**, 241.
[18] Werner, *Annalen*, 1912, **386**, 89.

the complex ion can still undergo aquation when absorbed in the ion-exchange resin, it was necessary to surround the resin column by ice–water and to flush the resin continually with water between each separation. Spectrophotometric measurements were made with silica cells and a Unicam S.P. 500 quartz spectrophotometer. Conductivities were measured on a Wayne–Kerr universal bridge B 221. The shiny platinum electrodes were in contact with the solution throughout the reaction.

Although no tests were made to see whether light affected the reaction it was excluded as routine.

One of the authors (S. C. C.) acknowledges an award from the Commonwealth Scholarship Commission.

William Ramsay and Ralph Forster Laboratories,
University College, Gower Street, London, W.C.1. [*Received, May 18th*, 1961.]

---

908. Solanum *Alkaloids. Part XV.*[1] *The Constituents of Some* Solanum *Species and a Reassessment of Solasodamine and Solauricine.*

By Lindsay H. Briggs, R. C. Cambie, and J. L. Hoare.

The glycosidic alkaloids of the fruit of eight members of the morellae section, and four others, of the *Solanum* species, have been shown by paper chromatography to contain solasonine and solamargine. Diosgenin has been isolated from the fruit of *S. auriculatum* Ait.

Further work has shown that solasodamine is solasonine monohydrate, solauricine is a mixture of solasonine and solamargine, and that solauricidine is probably a complex of solasodine and its galactoside.

The pigments of the ripe fruit of four *Solanum* species and the flowers of one have been identified as petanin and delphanin.

In a continuation of our investigations of the glycosidic alkaloid constituents of *Solanum* species [2] the green berries of eight plants belonging to the section morellae have been examined by paper chromatography with Paseshnichenko and Guseva's solvent system.[3] The results are reported in Table 1.

The yield of crude alkaloid varied considerably but the major constituents in each case

Table 1.

(A) = Solamargine; (B) = solasonine; (C) = β- and (D) = α-"solanigrine." Relative strengths of spots estimated visually on a weak (+) to strong (+++) basis. R_{as} = R for α-solanine.

Species	Source	Herbarium no.*	Yield (%)	(A) R_{as} 2·5	(B) R_{as} 1·3	(C) R_{as} 0·5	(D) R_{as} 0·2
Section: morellae							
S. americanum Mill.	U.S.A.	69,340	0·3	+++	+++	+	+
S. furcatum L.	Chile	69,338	0·6	+++	+++	+	+
S. "gsoba"	Unknown	69,343	0·6	+++	+++	+	+
S. interandinum Bitt. ...	Ecuador	69,341	0·2	+++	+++	+	+
S. melanocerasum All. ...	Denmark	69,345	0·1	+++	+++	(+)	(+)
S. nigrum L.	New Zealand	—	0·4	+++	+++	++	+
S. roxburghii Dun.....	India	69,346	0·7	+++	+++	++	+
S. sarachoides Sendtner...	U.S.A.	69,344	0·5	+++	+++	++	+
S. villosum Dun.	Denmark	69,342	0·1	+++	+++	+	+
S. aviculare Forst.	New Zealand	—	0·6	+++	+++	+	
S. ciliatum Lam.	Costa Rica	69,347	0·3	+++	+++		
S. integrifolium Poir	Unknown	—	0·2	+++	+++	+	
S. rostratum Dun.	U.S.A.	69,339	0·1	++	++		
S. vescum F. Muell.	Australia	—	0·9	+++	+++		

* No. of a leaf sample lodged in the herbarium of the Auckland Institute and Museum.

[1] Part XIV, Briggs, Colebrook, Miller, and Sato, *J.*, 1960, 3417.
[2] Briggs and Cambie, *J.*, 1958, 1422, and preceding papers.
[3] Paseshnichenko and Guseva, *Biokhimiya*, 1956, **21**, 585.

XUM

were shown to be solasonine and solamargine by chromatographic comparison with authentic samples. The same alkaloids were also shown to be present in four species belonging to other sections and their presence confirmed in the previously investigated species, *S. nigrum* L.[2,4,5] and *S. aviculare* Forst.[2,6] The presence of the principal alkaloid solasonine in *S. vescum* was confirmed by isolation, analysis, and hydrolysis to solasodine.

In addition to those corresponding to solasonine and solamargine weak spots corresponding to α- and β-" solanigrines," isolated from some species of the *S. nigrum* group by Schreiber,[5] were often observed and are probably due to the presence of different tetrasaccharides of solasodine. Although all berries were extracted by the improved method in which enzymic hydrolysis has been minimised,[7] with a few species traces of faster-moving spots were detected which could possibly correspond to fragments of enzymically hydrolysed solasonine or solamargine.

" *Solasodamine.*"—The green berries of *S. auriculatum*, *S. sodomaeum*, and *S. marginatum* were earlier reported[7] to contain solasodamine, a tetrasaccharide of solasodine, the glycosidic moiety of which contained glucose (1 mol.), galactose (1 mol.), and rhamnose (2 mols.), but repeated attempts to isolate further solasodamine from *S. auriculatum* gave solasonine as the major alkaloid with solamargine shown also to be present by paper chromatography. Paseshnichenko and Guseva's solvent system,[3] which was only available after the completion of the earlier work, was here used and in our experience is capable of differentiating mono-, di-, and tri-saccharides in this series. As these have decreasing R_F values, a tetrasaccharide would be expected to have an even lower R_F value. Solasodamine, however, has an R_F value identical with that of solasonine while solasonine, solamargine, and solanine (all with trisaccharide moieties) were readily resolved.

Re-examination (see Experimental section) has now convinced us that solasodamine is solasonine monohydrate and its name should, therefore, be discontinued.

" *Solauricine* " *and* " *Solauricidine.*"—Earlier, the isolation of a supposedly new glycoalkaloid, solauricine, from the dried berries of *S. auriculatum*, was reported.[8] Solauricine differed significantly from solasonine only in that the melting point (222—223°) of the derived alkamine, solauricidine, was higher than that of solasodine (200·5—202·5°). Attempts to reisolate solauricine and solauricidine from dried or fresh berries from monthly samples have been unsuccessful but samples of solauricidine regenerated from its salts still had m. p. 216—219°.

Re-examination of the original small samples by paper chromatography now indicates (see Experimental section) that " solauricidine " was a mixture of solasodine and its galactoside.

In addition, diosgenin has been isolated from the green berries. This has previously been reported from *S. xanthocarpum*[9] and *S. aviculare*.[10]

Pigments.—Two pigments from the ripe berries of *S.* " *gsoba* " were investigated by chromatographic methods.[11] R_F values in four solvent systems and the ultraviolet spectra were identical with those recorded for petanin and delphanin.[11] That the pigments were acylated followed from the chromatographic behaviour; a peak in the ultraviolet spectrum at 310 mμ indicated that the acyl component was *p*-coumaric acid (*p*-hydroxycinnamic acid).[12] Acid hydrolysis of the purified pigments and chromatography gave petunidin as the major anthocyanidin and smaller amounts of delphinidin, *p*-coumaric acid, glucose, and rhamnose, the former sugar occurring in double the concentration of

[4] Boll, *Acta Chem. Scand.*, 1958, **12**, 358.
[5] Schreiber, *Planta Med.*, 1958, **6**, 435.
[6] Kuhn, Löw, and Trischmann, *Chem. Ber.*, 1955, **88**, 289.
[7] Briggs and Brooker, *J.*, 1958, 1419.
[8] Anderson and Briggs, *J.*, 1937, 1036; Bell, Briggs, and Carroll, *J.*, 1942, 12.
[9] Sato and Latham, *J. Amer. Chem. Soc.*, 1953, **75**, 6067.
[10] Schreiber, " Sonderabduck aus Abhandlungen der deutschen Akademie der Wissenschaften zu Berlin," 1957, October.
[11] Harborne, *Biochem. J.*, 1960, **74**, 262 and preceding papers; *J. Chromat.*, 1958, **1**, 473.
[12] Harborne, *Biochem. J.*, 1958, **70**, 22.

the latter. A small spot corresponding to arabinose was also observed but Harborne and Sherratt [13] have pointed out that paper chromatography with solvents containing hydrochloric acid can produce arabinose as an artifact. The report that petanin, accompanied by traces of delphanin, is of widespread occurrence in plants of the Solanaceæ [11] supports the identification of the pigments in the present case. A similar investigation showed that the same pigments are present in the ripe berries of *S. americanum*, *S. interandinum*, and *S. intrusum*, and the flowers of *S. auriculatum*.

Experimental

Analyses are by Dr. A. D. Campbell, University of Otago, New Zealand, samples being dried at 100° to constant weight. *X*-Ray powder photographs were measured by using Pyrex capillaries and copper-*K* radiation. The crude alkaloids were isolated from green berries as previously described.[2] The species examined were germinated from seed in sterilised soil at 70° F and grown under controlled conditions.

Chromatography of Solanum *Alkaloids*.—Whatman's No. 1 paper, equilibrated for 12 hr., was used throughout with the following solvent systems: A (for glycosides), ethyl acetate–acetic acid–water (11 : 2 : 1·85; to give a homogeneous mixture; cf. ref. 3). In addition the system ethyl acetate–pyridine–water (3 : 1 : 3) was employed for comparison of R_{GA} values with those obtained by Schreiber for α- and β-"solanigrine"; [5] B (for alkamines), benzene–chloroform (1 : 2) saturated with formamide (stabilised with 1% v/v of light petroleum) on paper impregnated with formamide–acetone (3 : 7).[14] Iodine in light petroleum solution and a 25% solution of antimony trichloride in chloroform were used as sprays. With solvent A the following R_{GA} values were recorded: solanine 1·0; solasonine 1·3; solamargine 2·3; solasodine glucosylgalactoside * 2·5; solasodine rhamnosylglucoside 5·0; [15] solasodine glucoside 10·0, R_F 0·40; solasodine 15·0; R_F 0·76; solanidine 14·0, R_F 0·73. With solvent B the following R_F values were recorded: solasodine 0·5; solanidine 0·3; solasodine glucoside and solasonine 0·0.

The sugars from hydrolysis were examined as previously described.[2,7]

S. vescum.—*Isolation of solasonine*. The crude alkaloid (4·2 g.) from green berries (464 g.) was purified by repeated precipitation from boiling 3% acetic acid solution with ammonia. Repeated crystallisation from aqueous methanol (50%) gave needles, m. p. 298—302° (decomp.), which gave a single spot on the chromatogram corresponding to solasonine (Found: C, 61·3; H, 8·65; N, 1·7. Calc. for $C_{45}H_{73}NO_{16}$: C, 61·1; H, 8·3; N, 1·6%) [picrolonate, needles, m. p. 234° (decomp.) (Found: C, 57·1; H, 7·2; N, 6·2. Calc. for $C_{45}H_{73}NO_{16}.C_{10}H_8N_4O_5$: C, 57·5; H, 7·1; N, 6·1%)].

Hydrolysis of solasonine in the usual manner [2] gave solasodine, m. p. and mixed m. p. 199—200°. Comparative paper chromatography of the concentrated sugar solution showed the presence of galactose, glucose, and rhamnose.

S. auriculatum.—*Isolation of diosgenin*. The mixed glycosides (10 g.) from green berries (4·5 kg.), containing solasonine, solamargine, and a trace of a further alkaloid (R_{GA} 0·5), were hydrolysed in the usual manner, and the precipitated solasodine hydrochloride was washed with water and ether. Ether removed from the aqueous filtrate a gum which was chromatographed in chloroform on alumina (Spence and Co., grade H). Crystallisation of fractions eluted with chloroform gave diosgenin (40 mg.) which separated from acetone as needles, m. p. and mixed m. p. 203—206° (Found: C, 77·9; H, 10·1. Calc. for $C_{27}H_{42}O_3$: C, 78·2; H, 10·2%) (correct infrared spectrum). The acetate crystallised from acetone in rods, m. p. and mixed m. p. 197—198·5° (Found: C, 75·9; H, 9·8; Ac, 9·6. Calc. for $C_{29}H_{44}O_4$: C, 76·3; H, 9·7; Ac, 9·4%).

Treatment of an aqueous suspension of solasodine hydrochloride with aqueous ammonia (*d* 0·88) for 1 hr. at 100° gave solasodine, which on crystallisation from methanol had m. p. and mixed m. p. 199—201°.

The basified mother-liquors (600 c.c.) were extracted with chloroform and the extracts

* Unpublished work.

[13] Harborne and Sherratt, *Experientia*, 1957, **13**, 486.
[14] Tuzson, *Naturwiss.*, 1956, **43**, 198.
[15] Briggs, Tagungsberichte der Internationales Symposium über Chemie und Biochemie der Solanum-Alkaloide, Berlin, June 1959.

XUM

washed, dried, and concentrated to dryness *in vacuo*. The amorphous residue was chromatographed in chloroform on activated alumina, 100-c.c. fractions being eluted with chloroform. The combined residues from fractions 3—6 were washed with a little benzene and recrystallised from acetone, to give solasodiene (140 mg.) as rectangular plates, m. p. and mixed m. p. 177—178° (Found: C, 82·0; H, 10·6; N, 3·3. Calc. for $C_{27}H_{41}NO$: C, 82·0; H, 10·45; N, 3·5%). The hydrochloride prepared by passing hydrogen chloride into an 80% aqueous ethanol solution had m. p. 318—320° (decomp.) [lit.,[16] m. p. 318° (decomp.)] (Found: C, 75·1; H, 10·2. Calc. for $C_{27}H_{41}NO,HCl$: C, 75·0; H, 9·8%).

Leaves of S. auriculatum.—Fresh green leaves (820 g.) worked up in the usual manner gave crude mixed alkaloids (5·0 g.) containing solasonine (R_{GS} 1·3) and solamargine (R_{GS} 2·5).

Berries of S. auriculatum.—(*a*) The alkaloids (7·5 g.) isolated in the normal manner from dried berries (1·65 kg.) contained solasonine (R_{GS} 1·3, strong), solamargine (R_{GS} 2·5, strong), and two alkaloids (R_{GS} 0·5, weak; and 5·8, strong).

(*b*) Ripe yellow berries (2·6 kg.) were coarsely crushed, made into a slurry with water, covered with toluene, and left to ferment for 4 months. The slurry was mixed with Celite and filtered. Precipitation of the alkaloids with ammonia and working up in the usual manner with separation from considerable inorganic matter gave crude bases, containing solasonine (R_{GS} 1·3, very weak) and an alkaloid (R_{GS} 0·5, very weak).

Re-examination of " Solasodamine."—No significant difference exists between the recorded physical properties of solasodamine and solasonine or of their respective derivatives. The analytical requirements for solasodamine (Calc. for $C_{51}H_{83}NO_{20}$: C, 59·5; H, 8·1; N, 1·4%) are very similar to those for solasonine monohydrate (Calc. for $C_{45}H_{73}NO_{16},H_2O$: C, 59·9; H, 8·4; N, 1·55%); the same applies to the picrates and picrolonates. The original samples of solasodamine for analysis were dried overnight at 100° over phosphorus pentoxide. Samples of solasodamine dried to constant weight at 100° have now given analytical figures in agreement with those for solasonine (Found: C, 61·3; H, 8·3; N, 1·4. Calc. for $C_{45}H_{73}NO_{16}$: C, 61·15; H, 8·3; N, 1·6%).

Solasodamine was found earlier on periodate oxidation to consume 6 mol./mol. and to produce 2 mol. of formic acid. When the calculations are re-interpreted on the basis of the molecular weight of solasonine (the samples oxidised were dried at 110° for 43 hr. *in vacuo* over magnesium perchlorate), the values become 5·0 and 1·8, respectively, in agreement with those found for solasonine.[17]

In the quantitative separation of the sugars liberated on hydrolysis of solasodamine it was reported that 2 mol. of rhamnose were produced. The rhamnose, eluted as the initial product from a cellulose column, was obtained only as a syrup which was dried to constant weight at 40° over magnesium perchlorate. Although the rhamnose was uncontaminated with other sugars it appears that significant amounts of impurity could have been eluted from the column or that the material was insufficiently dried. In subsequent experiments involving the chromatography of sugars on cellulose columns we found that impurities are still eluted from columns which had been pre-washed before use.

Further, as previously reported,[7] the infrared spectra of solasodamine and solasonine are indistinguishable but further measurements now show a slight difference between those of solasonine and solamargine. Finally, *X*-ray powder photographs of solasodamine and solasonine are identical but that of solamargine is different.

Solasonine " solasodamine " (5·1 g.), dried over magnesium perchlorate at 110°/0·01 mm. for 3 days, was heated under reflux with acetic anhydride (83 c.c.) and pyridine (1 c.c.) for 2 hr. The solution was concentrated to 25 c.c. *in vacuo* and treated with ice. The oil produced slowly solidified. Purification by repeated precipitation from alcohol with water, followed by repeated crystallisation from moist benzene, gave hygroscopic prisms of *deca-acetylsolasonine* (6·67 g.), m. p. 159·5—163° (decomp.) with sintering at 125° (Found: C, 60·0; H, 7·4; N, 1·0; Ac, 32·9. $C_{65}H_{93}NO_{26}$ requires C, 60·0; H, 7·2; N, 1·1; 10Ac, 33·0%).

Re-examination of " Solauricine " and " Solauricidine."—Solauricine gave a major spot identical with that of solasonine and a minor spot corresponding to solamargine, a compound now shown to co-exist in the berries. Reversed-phase paper chromatography of analytical samples of solauricidine showed a major spot corresponding to solasodine, and a spot at the origin corresponding to glycosidic material. When a solvent system capable of resolving

[16] Briggs, Newbold, and Stace, *J.*, 1942, 3.
[17] Briggs and Vining, *J.*, 1953, 2809.

glycosides was used this impurity appeared as a spot corresponding to a solasodine monosaccharide. This was then shown to be solasodine galactoside since hydrolysis of the sample and chromatographic examination of the sugars showed a faint spot corresponding to galactose (it will be shown later that in solasonine galactose is directly joined to the alkamine, as in solanine). Single crystals of solauricidine, however, on the micro-stage showed no sign of melting around 200° (the m. p. of solasodine), but softened and gradually shrank above 212° with melting at 218—222°, varying somewhat from crystal to crystal. Although insufficient material remains to resolve the problem unambiguously it appears that solauricidine is a complex of solasodine and solasodine galactoside resulting from incomplete hydrolysis.

Examination of the Anthocyanins.—The general method of isolation, separation, and purification of pigments, and the conditions used for spectroscopy and paper chromatography, were those recorded by Harborne for petanin and delphanin.

To isolate the pigments from *S.* "*gsoba*" chromatography was initially carried out in Harborne's solvent A,[11] followed by rechromatography in Harborne's solvents B and C,[11] on Whatman No. 3MM paper until the pigments were free from visible impurities and substances fluorescing in ultraviolet light. At each purification the pigments were eluted from the paper with acetic acid–methanol–water (5 : 70 : 25) in Canny's apparatus,[18] and the resulting extracts were concentrated *in vacuo* at room temperature.

After acid hydrolysis [11] of the pigments, comparative paper chromatography and spectroscopic examination showed the presence of petunidin, delphinidin [Harborne's solvent B,[11] and formic acid–concentrated hydrochloric acid–water (5 : 2 : 3)], and glucose, rhamnose, and arabinose [butan-1-ol–pyridine–water (3 : 1 : 5, upper phase with 1 vol. of pyridine)].

Alkaline hydrolysis [11] and comparative chromatography showed the presence of *p*-coumaric acid (Harborne's solvent B).

We are indebted to Professor C. B. Heiser, Indiana University, for seeds of most of the species which were grown at the Plant Diseases Division, Department of Scientific and Industrial Research, Mt. Albert, through the very kind co-operation and assistance of Mr. J. A. Hunter, N.D.H. We thank Professor G. T. S. Baylis, University of Otago, for berries of *S. vescum*, Mr. R. L. Sinclair for *X*-ray powder photographs, and Mr. L. D. Colebrook for infrared measurements; also the Chemical Society, the Rockefeller Foundation of New York, the Australian and New Zealand Association for the Advancement of Science, and the Research Grants Committee of the University of New Zealand; one of us (J. L. H.) acknowledges the award of a Boots Research Fellowship and a Duffus Lubecki Fellowship.

Department of Chemistry, University of Auckland,
Auckland, New Zealand. [*Received, May 24th*, 1961.]

[18] Canny, *J. Chromat.*, 1960, **3**, 496.

---

909. *Ionophoresis of Carbohydrates. Part VII.* 2,5-Di-O-methyl-L-rhamnose: its Ionophoresis and Conversion into 6-Deoxy-2,5-di-O-methyl-L-altrose.*

By A. B. Foster, J. Lehmann, and M. Stacey.

A synthesis of 2,5-di-*O*-methyl-L-rhamnose is described. It is the first example of a sugar derivative the mobility of which in ionophoresis in borate buffer (pH 10) is due solely to complex formation of the aldehydo-form with borate ions. The conversion of 2,5-di-*O*-methyl-L-rhamnose into 6-deoxy-2,5-di-*O*-methyl-L-altrose is also described.

In order to rationalise the pattern of mobilities (M_G values) of a range of methylated sugars in ionophoresis in a borate buffer at pH 10, it has been suggested [1] that aldehydo-forms, in addition to pyranose and furanose structures, form complexes with borate ions.

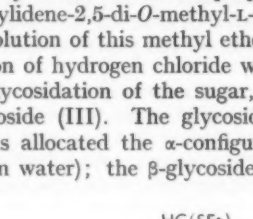
* Part VI, *J.*, 1957, 4214.

[1] Foster, *J.*, 1953, 982.

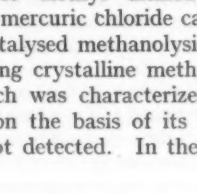
XUM

We now describe a synthesis of 2,5-di-*O*-methyl-L-rhamnose, the first example of a sugar derivative of which only the aldehydo-form gives rise to complexes with borate ions.

Treatment of L-rhamnose diethyl dithioacetal [2] with acetone, sulphuric acid, and anhydrous copper sulphate [3] afforded a mono-*O*-isopropylidene derivative (I) characterized as the di-*O*-*p*-phenylazobenzoate. From theoretical considerations,[4] acetone would be expected to condense with the 3,4-hydroxyl groups in L-rhamnose diethyl dithioacetal since they are αT (Barker and Bourne's nomenclature [5]). Proof of this was obtained as follows. Methylation of the *O*-isopropylidene derivative with dimethyl sulphate [6] gave 3,4-*O*-isopropylidene-2,5-di-*O*-methyl-L-rhamnose diethyl dithioacetal (II). Boiling a methanolic solution of this methyl ether with mercuric chloride caused demercaptalation with liberation of hydrogen chloride which catalysed methanolysis of the isopropylidene group and glycosidation of the sugar, affording crystalline methyl 2,5-di-*O*-methyl-α-L-rhamnofuranoside (III). The glycoside, which was characterized as the *p*-phenylazobenzoate, was allocated the α-configuration on the basis of its high negative rotation ($[\alpha]_D$ −110° in water); the β-glycoside was not detected. In the β-glycofuranoside, the



(I) R = H
(II) R = Me



(III) R = Me
(IV) R = H

1- and 2-methoxy-groups would be *cis*-disposed and the adverse non-bonded interaction associated with this steric arrangement probably accounts for the stereospecific formation of the α-glycoside which is free from such a steric effect. It is of interest that the isomers which predominate in the mixture of glycosides formed when erythrose and threose are separately treated with methanolic hydrogen chloride also have a *trans*-disposition of the 1-methoxyl and 2-hydroxyl group.[7] However, in the alternative isomers, these groups are *cis*-disposed and the intramolecular hydrogen bonding consequently possible could help to stabilise these isomers and this would reduce the stereospecificity of the glycosidation. Hydrogen bonding of this type cannot occur in the L-rhamnoside derivatives.

Acid hydrolyses the glycoside (III) to 2,5-di-*O*-methyl-α-L-rhamnofuranose (IV), the α-configuration being allocated on the basis of the mutarotational changes in water, $[\alpha]_D$ −61° (30 min.) ⟶ −41°. Sodium borohydride reduced the free sugar (IV) to 2,5-di-*O*-methyl-L-rhamnitol which consumed 1 mol. of periodate, giving products which when reduced with sodium borohydride and esterified afforded 2-*O*-methyl-1,3-di-*O*-*p*-phenylazobenzoylglycerol. Only a 2,5-distribution of methyl groups in the L-rhamnitol derivative permits formation of 2-*O*-methylglycerol in this reaction sequence. Determination of the structure of 2,5-di-*O*-methyl-L-rhamnitol also establishes the structures of all the preceding compounds (I)—(IV). Authentic 2-*O*-methyl-1,3-di-*O*-*p*-phenylazobenzoylglycerol was obtained from 2-methoxy-5-phenyl-1,3-dioxan [8] by acidic hydrolysis and subsequent esterification.

2,5-Di-*O*-methyl-L-rhamnose had M_G 0·20 on ionophoresis in a borate buffer pH 10. The sugar can exist only in furanose and aldehydo-forms in aqueous solution and, if hydration of the carbonyl group in the open-chain form is assumed, then, since terdentate

[2] Fischer, *Ber.*, 1894, **27**, 678.
[3] Curtis and Jones, *Canad. J. Chem.*, 1960, **38**, 890.
[4] Barker, Bourne, and Whiffen, *J.*, 1952, 3865; Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[5] Barker and Bourne, *J.*, 1952, 905.
[6] Glen, Myers, and Grant, *J.*, 1951, 2568.
[7] Baxter and Perlin, *Canad. J. Chem.*, 1960, **38**, 2217.
[8] Hill, Whelen, and Hibbert, *J. Amer. Chem. Soc.*, 1928, **50**, 2235.

complexes [9] are precluded, the pairs of hydroxyl groups available for borate complex formation are as follows: furanose form, *cis*- and *trans*-1,3; aldehydo-form, 3,4(αT), 1,3(β), and 1,4(γ). Complex formation with the furanose form can be ruled out because of the large O–O distances for the hydroxyl groups (*ca.* 3·5 Å for the *cis*-diol). Likewise a complex with the γ-hydroxyl groups in the open-chain form can be discounted since 1,4-diols do not react with borate ions.[10] The fact that 2,4-di-*O*-methyl derivatives of D-galactose [11] and D-glucose [1] have zero M_G values indicates that borate complex formation with carbonyl and a β-hydroxyl group does not occur since this structural feature is present in the aldehydo-forms of these compounds. This leaves only the αT hydroxyl groups in the open-chain form of 2,5-di-*O*-methyl-L-rhamnose for complex formation with borate ions. Frahn and Mills [10] have shown that borate ions form complexes more readily with αT than with αC or α hydroxyl groups (L-*threo*butane-2,3-diol M_G 0·51, *erythro*-isomer M_G 0·13, propane-1,2-diol M_G 0·16). Thus it may be predicted that 6-deoxy-2,5-di-*O*-methyl-L-altrose, which has the same possibilities for borate complex formation as 2,5-di-*O*-methyl-L-rhamnose (except that αC instead of αT hydroxyl groups are available in the aldehydo-form) would have an M_G value much lower than 0·2. The observed M_G value was zero.

6-Deoxy-2,5-di-*O*-methyl-L-altrose was synthesised as follows. The crystalline *O*-methanesulphonate of methyl 2,4-di-*O*-methyl-α-L-rhamnofuranoside with sodium benzoate in dimethylformamide gave methyl 3-*O*-benzoyl-6-deoxy-2,5-di-*O*-methyl-α-L-altrofuranoside. Nucleophilic displacement of sulphonyl groups with concomitant Walden inversion by this reagent has been described by Reist *et al.*[12] Saponification of the benzoate and acidic hydrolysis of the product gave 6-deoxy-2,5-di-*O*-methyl-L-altrose, which, although not crystalline, was homogeneous on paper chromatography and had the same R_F value as 2,5-di-*O*-methyl-L-rhamnose.

Experimental

3,4-O-*Isopropylidene*-L-*rhamnose Diethyl Dithioacetal*.—A mixture [3] of L-rhamnose diethyl dithioacetal [2] (30 g.; m. p. 135—137°), anhydrous copper sulphate (20 g.), concentrated sulphuric acid (3 ml.), and acetone (550 ml.) was shaken at room temperature for 6 hr. The acid was then neutralised with concentrated aqueous ammonia, and insoluble material was removed by filtration and washed with acetone. The combined filtrate and washings were concentrated, and the residue was dissolved in chloroform and washed with water, aqueous sodium hydrogen carbonate, and water. Evaporation of the dried ($MgSO_4$) solution and distillation of the residue gave the *product* (28 g., 81%), b. p. 148—152°/0·5 mm., $[\alpha]_D^{22}$ −31° (*c* 4·0 in $CHCl_3$), $[M]_D$ −96° (Found: C, 50·5; H, 8·1; S, 20·3. $C_{13}H_{26}O_4S_2$ requires C, 50·3; H, 8·4; S, 20·7%).

Treatment of this compound (1·55 g.) with *p*-phenylazobenzoyl chloride (2·67 g.) and pyridine (10 ml.) at 100° for 3 hr. and isolation of the product in the usual way [13] gave a 2,5-*di*-O-p-*phenylazobenzoate* (1·9 g., 62%) m. p. 118—119° [from benzene–light petroleum (b. p. 60—80°)] (Found: C, 64·7; H, 5·9; N, 7·5; S, 8·6. $C_{39}H_{42}N_4O_6S_2$ requires C, 64·5; H, 5·8; N, 7·7; S, 8·8%).

3,4-O-*Isopropylidene*-2,5-*di*-O-*methyl*-L-*rhamnose Diethyl Dithioacetal*.—A solution of 3,4-*O*-isopropylidene-L-rhamnose diethyl dithioacetal (4·61 g.) in acetone (7·5 ml.) was stirred vigorously with powdered sodium hydroxide [6] (3·2 g.) at 45—48° whilst dimethyl sulphate (4·2 ml.) was added during 30 min. The temperature of the mixture was then raised to 55—60° during 30 min. and maintained thereat for 3 hr. The cooled mixture was poured into water, and the aqueous solution was extracted several times with chloroform. The combined extracts were washed with water, dried ($MgSO_4$), and concentrated and the residue was distilled, to

[9] Angyal and McHugh, *Chem. and Ind.*, 1956, 1147.
[10] Frahn and Mills, *Austral. J. Chem.*, 1959, **12**, 65.
[11] Lindberg and Swan, *Acta Chem. Scand.*, 1960, **14**, 1043.
[12] Reist, Spencer, and Baker, *J. Org. Chem.*, 1959, **24**, 1618.
[13] Baggett, Foster, Haines, and Stacey, *J.*, 1960, 3528.

yield the *product* (3·9 g., 78%) as a pale yellow oil, b. p. 118—122°/0·5 mm., $[\alpha]_D^{20}$ −34° (*c* 2·0 in $CHCl_3$), $[M]_D$ −115° (Found: C, 54·1; H, 9·1; S, 19·1. $C_{15}H_{30}O_4S_2$ requires C, 53·3; H, 8·9; S, 18·9%).

Methyl 2,5-*Di*-O-*methyl*-α-L-*rhamnofuranoside*.—3,4-*O*-Isopropylidene-2,5-di-*O*-methyl-L-rhamnose diethyl dithioacetal (5·4 g.) was boiled with mercuric chloride (11·6 g.) in dry methanol (95 ml.) under anhydrous conditions for 30 min., then filtered quickly, and the filtrate was evaporated. The residue was extracted with 10% aqueous sodium carbonate (200 ml.), and the extract was filtered and extracted with chloroform (4 × 100 ml.). The chloroform extracts were washed with water, dried ($MgSO_4$), and evaporated. Crystallization of the residue from ether–light petroleum (b. p. 40—60°) gave the *product* (2 g., 61%), m. p. 63—65°, b. p. 83—84°/0·5 mm., $[\alpha]_D^{20}$ −110° (*c* 1·5 in H_2O), $[M]_D$ −227° (Found: C, 52·25; H, 8·7. $C_9H_{18}O_5$ requires C, 52·4; H, 8·7%).

Esterification of the glycoside (0·2 g.) with pyridine (3 ml.) and *p*-phenylazobenzoyl chloride (0·265 g.) in the customary manner [13] gave the O-p-*phenylazobenzoate* (0·39 g.), m. p. 87° (from aqueous ethanol) (Found: C, 64·0; H, 6·2; N, 6·8. $C_{22}H_{26}N_2O_6$ requires C, 63·8; H, 6·3; N, 6·8%).

The glycoside, with methanesulphonyl chloride and pyridine in the usual way, gave the 3-O-*methanesulphonate* (58%), m. p. 36—37°, $[\alpha]_D$ −64° (*c* 1·2 in $CHCl_3$), $[M]_D$ −182° (Found: C, 42·2; H, 7·05; S, 11·2. $C_{10}H_{20}O_7S$ requires C, 42·3; H, 7·0; S, 11·3%).

2,5-*Di*-O-*methyl*-L-*rhamnose*.—A solution of methyl 2,5-di-*O*-methyl-α-L-rhamnofuranoside (1 g.) in 2N-hydrochloric acid (30 ml.) was kept at 100° for 2·5 hr., then neutralised with sodium hydrogen carbonate and extracted continuously with chloroform. The dried ($MgSO_4$) extract was concentrated and the residue recrystallized to yield 2,5-*di*-O-*methyl*-L-*rhamnose* (0·8 g., 84%), m. p. 94—95°, $[\alpha]_D$ −61° (30 min.) ⟶ −41° (equil.) (*c* 2·0 in H_2O), $[M]_D$ −117° ⟶ −79° (Found: C, 50·2; H, 8·6. $C_8H_{16}O_5$ requires C, 50·0; H, 8·3%), that reduced Fehling's solution and had M_G 0·20 on paper ionophoresis [1,14] in borate buffer of pH 10.

2,5-*Di*-O-*methyl*-L-*rhamnitol*.—A solution of 2,5-di-*O*-methyl-L-rhamnose (0·23 g.) and sodium borohydride (50 mg.) in water (15 ml.) was kept at room temperature for 8 hr., then neutralised with acetic acid to destroy the excess of reductant. The solution was basified with 20% aqueous sodium hydroxide (50 ml.) and continuously extracted with chloroform during 3 days. Concentration of the dried ($MgSO_4$) extract and recrystallization of the residue from acetone–ether gave the *product* (0·18 g., 78%), m. p. 71—72·5°, $[\alpha]_D$ +27° (*c* 2 in H_2O), $[M]_D$ +52° (Found: C, 49·55; H, 9·4. $C_8H_{18}O_5$ requires C, 49·5; H, 9·3%).

Periodate Oxidation of 2,5-*Di*-O-*methyl*-L-*rhamnitol*.—(*a*) By a standard method [15] the L-rhamnitol derivative was found to consume 1 mol. of periodate.

(*b*) A solution of 2,5-di-*O*-methyl-L-rhamnitol (0·2 g.), sodium metaperiodate (0·45 g.), and sodium hydrogen carbonate (0·17 g.) in water (5 ml.) was kept at room temperature for 5 hr. Iodate and periodate were precipitated by the addition of barium chloride, and sodium borohydride (100 mg.) was then added to the filtered solution. After 16 hr. the excess of reductant was destroyed with acetic acid and the solution, after basification with 20% aqueous sodium hydroxide (20 ml.), was continuously extracted with chloroform for 4 days. The dried ($MgSO_4$) extract was concentrated and the residue was treated with *p*-phenylazobenzoyl chloride (0·5 g.) and pyridine (4 ml.) at 100° for 3 hr. Working up in the usual way [13] yielded 2-*O*-methyl-1,3-di-*O*-*p*-phenylazobenzoylglycerol (0·38 g., 63%), m. p. 129° alone or in admixture with material described below. The infrared spectrum (Nujol mull) was indistinguishable from that of the authentic compound.

No trace of the *p*-phenylazobenzoate of the second reaction product, 2-methoxypropan-1-ol, was detected. Presumably the alcohol was lost by volatilization.

2-O-*Methyl*-1,3-O-p-*phenylazobenzoylglycerol*.—2-*O*-Methylglycerol [8] (0·1 g.) when esterified [13] with pyridine (4 ml.) and *p*-phenylazobenzoyl chloride (0·53 g.) gave the *diester* (0·49 g., 81%), m. p. 129—130° (from ethanol) (Found: C, 69·05; H, 5·3; N, 10·8. $C_{30}H_{26}N_4O_5$ requires C, 69·0; H, 5·0; N, 10·7%).

Methyl 6-*Deoxy*-2,5-*di*-O-*methyl*-α-L-*altrofuranoside*.—A solution of methyl 3-*O*-methanesulphonyl-2,5-di-*O*-methyl-α-L-rhamnofuranoside (1·5 g.) in dimethylformamide (64 ml.) was boiled under reflux in the presence of sodium benzoate (5·2 g.) for 6 hr., then poured into water and the solution extracted with chloroform. The extract was washed with aqueous sodium

[14] Foster, *Chem. and Ind.*, 1952, 1050.
[13] Jackson, *Org. Reactions*, 1944, **2**, 341.

hydrogen carbonate and with water, dried ($CaCl_2$), and evaporated. Distillation of the residue gave methyl 3-*O*-benzoyl-6-deoxy-2,5-di-*O*-methyl-α-L-altrofuranoside (0·95 g., 58%) contaminated with a small amount of starting material. The product had b. p. 124—126°/0·1 mm., $[\alpha]_D$ −105° (*c* 1·2 in $CHCl_3$).

A solution of this product (0·5 g.) in methanol (12 ml.) and water (18 ml.) containing potassium hydroxide (4 g.) was boiled under reflux for 3 hr., cooled, and extracted four times with chloroform (total vol. 100 ml.), and the combined extracts were washed with water and evaporated. The residue (0·27 g.) was distilled, to yield *methyl 6-deoxy-2,5-di-O-methyl-α-L-altrofuranoside*, b. p. 100—110°/0·1 mm., $[\alpha]_D$ −85° (*c* 2·0 in H_2O), $[M]_D$ −175° (Found: C, 52·7; H, 8·55. $C_9H_{18}O_5$ requires C, 52·4; H, 8·7%).

A solution of the glycoside (0·2 g.) in 2N-hydrochloric acid (10 ml.) was boiled under reflux for 3 hr., then neutralised and continuously extracted with chloroform. The extract was concentrated and a solution of the residue in water (50 ml.) was extracted with chloroform (2 × 40 ml.). Concentration of the aqueous solution gave 6-deoxy-2,5-di-*O*-methyl-L-altrose (90 mg.), $[\alpha]_D$ −16° (*c* 1·2 in H_2O). The compound failed to crystallize but appeared homogeneous on paper chromatography with the organic phase of a butanol–ethanol–water (4 : 1 : 5) solvent system; it had R_G 5·29 and R_{Rh} 2·17. On ionophoresis [14] in borate buffer pH 10 it had $M_G < 0{\cdot}01$.

One of the authors (J. L.) thanks the Duisberg Stiftung for a grant.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, April 12th,* 1961.]

---

910. *The Catalytic Action of Anionic Catalysts. Part I. The Interaction of Butyl-lithium with* 1,1-*Diphenylethylene.*

By ALWYN G. EVANS and DAVID B. GEORGE.

Butyl-lithium with 1,1-diphenylethylene in benzene gives the ion pair $Bu{\cdot}CH_2{\cdot}CPh_2^-Li^+$, which has an absorption peak at 428 mμ (ε 1·6 × 10^4). The order of this reaction is unity in 1,1-diphenylethylene, and 0·18 in butyl-lithium. Since it is known that butyl-lithium is highly associated (some six-fold) in benzene, we interpret the low order in this reagent by assuming (i) that equilibrium in this association lies well towards the associated side, and (ii) that only monomeric butyl-lithium reacts with 1,1-diphenylethylene.

Butyl-lithium does not react with 1,1,3,3-tetraphenylbut-1-ene or with tetraphenylethylene, although both these olefins give carbonium ions with dilute acids. We assume that steric hindrance here inhibits formation of an anion by addition of a butyl group.

THE action of cationic catalysts on 1,1-diphenylethylene was studied earlier; [1] we have extended this work to anionic catalysts. Following a preliminary communication [2] this paper gives a detailed account of the spectrophotometric part of this work.

EXPERIMENTAL

Apparatus.—The apparatus used was of all-glass construction, without taps. Contamination with tap grease or air was impossible. The glass was cleaned by soaking it for a few minutes in concentrated nitric acid, followed by a rinse with water and a soaking for some minutes in 5% aqueous sodium hydroxide; it was then washed in a stream of water for at least an hour, and after a final rinse with distilled water was dried in an oven at 120°. Each piece of apparatus was baked under a high vacuum for at least 3 hr. before contact with any of the reagents.

[1] Evans and E. D. Owen, *J.*, 1959, 4123.
[2] Evans and George, *Proc. Chem. Soc.*, 1960, 144.

The optical cells used were of Pyrex glass and were cylindrical with optically flat ends separated by 1 cm.

Materials.—Benzene and 1,1,3,3-tetraphenylbut-1-ene were prepared and purified as described earlier.[3] 1,1-Diphenylethylene was purified by the rigorous treatment with stannic chloride described earlier.[4]

Tetraphenylethylene was prepared by the action of copper bronze on dichlorodiphenylmethane and, recrystallised from dioxan, had m. p. 221°.

" AnalaR " diethyl ether was dried over sodium wire, distilled, then outgassed under a high-vacuum and stored over sodium–potassium alloy in vessels fitted with magnetically operated breakers.

Benzyl chloride, after being dried (P_2O_5) and distilled at atmospheric pressure, was outgassed and then distilled a number of times under a high vacuum. The first and last 5% were discarded in each distillation.

A solution of butyl-lithium in benzene was prepared by the method of Ziegler and Colonius [5] adapted to high-vacuum conditions in a manner similar to that described by Evans and Owen.[6]

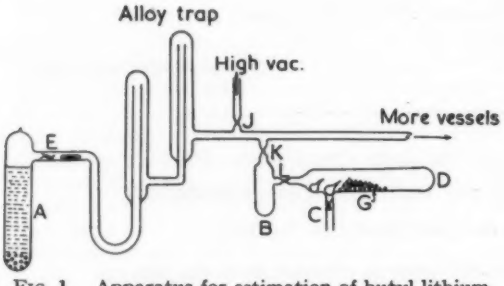


FIG. 1. Apparatus for estimation of butyl-lithium.

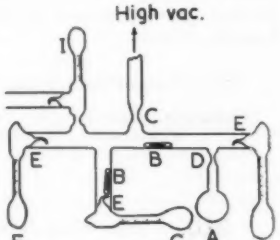


FIG. 2. Apparatus for preparation of reaction solution.

A, Optical cell. F, Benzene. G, Benzene solution of butyl-lithium. H, Benzene solution of 1,1-diphenylethylene. I, Vessel to collect excess of solution.

Standardisation of the Butyl-lithium Solution.—The double-titration method of Gilman and Haubein [7] was adapted to high-vacuum conditions as follows. Fragile bulbs of known volume were filled with the butyl-lithium solution under a high vacuum. They were then broken under distilled water, and the lithium hydroxide formed was titrated with standard hydrochloric acid to phenolphthalein.

Further samples of the butyl-lithium solution were pretreated with benzyl chloride in dry ether in the apparatus shown in Fig. 1. After a thorough baking under a high vacuum, the apparatus was opened at the point D and two bulbs were introduced, one containing a known volume of the butyl-lithium solution and the other a known volume of benzyl chloride. Glass beads, G, were also introduced. The apparatus was resealed at D and after evacuation was sealed from the pumps at J. The fragile capillary E was next broken by operating the magnetic breaker, and ether was distilled from vessel A, where it was over sodium–potassium alloy, into vessel B by cooling the latter in ice-water. When sufficient had collected (about 20 ml.), the vessel was sealed off at the constriction K. The ether was then poured into the adjoining vessel containing the bulbs of butyl-lithium and benzyl chloride, which was then sealed at L. The bulbs containing the reactants were next completely shattered by vigorously shaking the vessel. As the substances mixed an exothermic reaction ensued and a fleeting yellow colour

[3] Evans and Price, *J.*, 1959, 2982.
[4] Evans and Lewis, *J.*, 1957, 2975.
[5] Ziegler and Colonius, *Annalen*, 1930, **479**, 135.
[6] Evans and G. D. T. Owen, *J.*, 1961, 1733.
[7] Gilman and Haubein, *J. Amer. Chem. Soc.*, 1944, **66**, 1515.

appeared, which was quickly followed by a white precipitate. The whole was set aside for several minutes and capillary C was then broken and the solution was hydrolysed with distilled water. The mixture, with copious washings, was transferred to a titrating flask and the lithium hydroxide present was estimated as before, vigorous shaking being maintained throughout the titration to ensure thorough mixing of the ether and water layers. In this way it was found that the butyl-lithium solution contained less than 3% of impurities (see Table 1), and that the solution gave the same analysis after several months' storage at 6—7°.

General Procedure.—Benzene solutions of butyl-lithium and of olefin were mixed in the manner described below, and the ultraviolet absorption, D, of the resulting solution was measured at various time intervals at 428 mμ. All citations of D hereafter also refer to 428 mμ.

Master solutions of the monomer, 1,1-diphenylethylene,[4] and the linear dimer (1,1,3,3-tetraphenylbut-1-ene) [3] in benzene were prepared under high-vacuum conditions as described in earlier papers. The solution of tetraphenylethylene in benzene was prepared in a manner similar to that of the butene solution. Known volumes of these master solutions and of the butyl-lithium solution were diluted with known volumes of benzene, under high-vacuum conditions, until the resulting solutions were sufficiently dilute for use in preparing the solutions for reaction.

The reactants were mixed and the optical cells filled with the solution by using the apparatus shown in Fig. 2. After being baked under a high vacuum the apparatus was sealed at C. The bulbs, each containing a known volume of solution, were next opened to the central part of the apparatus by breaking the fragile capillaries, E, by means of the iron-in-glass breakers, B, and the solutions of olefin and of butyl-lithium in benzene, and benzene itself were quickly but thoroughly mixed. The reaction solution was then poured into the optical cell which was sealed at the constriction D. Together with a similar cell containing pure benzene as control, it was placed in a thermostat bath fitting on the carriage of a Unicam S.P.500 spectrophotometer. This thermostat bath was fitted with silica windows, and water at a known temperature (±0·1°) was circulated through it.

Results

Interaction of Butyl-lithium with 1,1-Diphenylethylene.—Spectrum. When benzene solutions of 1,1-diphenylethylene and butyl-lithium were mixed, a yellow colour appeared which gradually

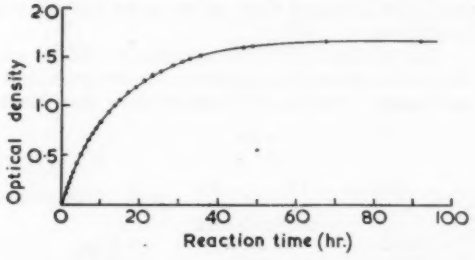


FIG. 3. A typical reaction rate plot.

Temp. 30·5°. $[BuLi]_i = 1·51 \times 10^{-3}$ mole l.$^{-1}$. $[CH_2{:}CPh_2]_i = 1·01 \times 10^{-4}$ mole l.$^{-1}$.

intensified until it became orange, or, if the solutions were very concentrated, a deep cherry-red. The optical density of such solutions increased with time to a value which remained constant for several days (see Fig. 3). The spectrum of a solution which has reached this steady state is given in Fig. 4, curve A. This curve is of the same shape as that given in our preliminary communication,[2] but the optical density is greater than that which we should expect from our earlier work. We believe this to be because in our earlier experiments the solution had been left for some time before dilution for spectroscopic measurement, and we now find a very slow decrease in optical density after the steady state has been reached. This decrease, however, is so slow that even after many months the reaction solutions are still coloured.

Order of reaction. Initial rates of formation of the coloured species were determined from tangents at the origin of the optical density–time plots. These tangents could be drawn with an accuracy of within 5%. The order of reaction in butyl-lithium was found from the dependence of the initial rate of reaction on the initial butyl-lithium concentration for a series of experiments in which the initial monomer concentration and the reaction temperature were

kept constant. These results (Table 2) show that an ~100-fold increase in the initial butyl-lithium concentration increases the initial rate only by about two-fold. The plot of $\log_{10}$ (initial rate = R_i) against $\log_{10}$ (initial butyl-lithium concentration = $[BuLi]_i$) shows the order of the reaction in butyl-lithium to be $0{\cdot}18 \pm 0{\cdot}02$ (see also column 4, Table 2).

Since a large excess of butyl-lithium over 1,1-diphenylethylene was used in each experiment, the order of reaction in the latter reagent could be obtained from an analysis of the optical density–time curves. Each of these shows the order of reaction in 1,1-diphenylethylene to be 1·0. An example of such an analysis is given in Table 3.

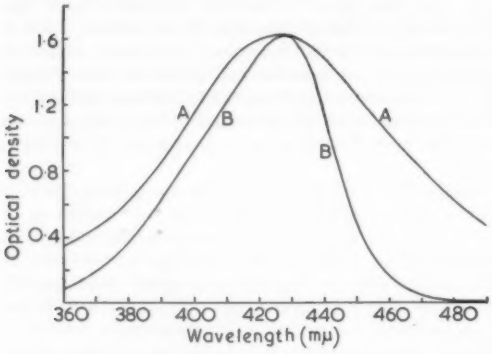


FIG. 4. (A) Benzene solution of LiBu ($1{\cdot}51 \times 10^{-2}$ mole $l.^{-1}$) and $CH_2{:}CPh_2$ ($1{\cdot}01 \times 10^{-4}$ mole $l.^{-1}$) at 20°. (B) $CH_2{:}CPh_2$ in 98% H_2SO_4 ($0{\cdot}58 \times 10^{-4}$ mole $l.^{-1}$) at 20°.

The dependence of the initial rate of reaction on initial 1,1-diphenylethylene concentration is shown in Table 4. It is again seen that the order in diphenylethylene is $1{\cdot}0 \pm 0{\cdot}05$.

Thus we may write:

$$\text{Rate of production of coloured species} = k[CH_2{:}CPh_2]^1[BuLi]^{0{\cdot}18}.$$

Irreversibility of reaction. The fact that first-order kinetics hold up to at least 96% reaction (see Table 3) shows that, as far as we can determine, the reaction is irreversible under these conditions.

Test of Beer's law. We allowed a reaction system to come to the steady state, and then diluted it with various quantities of benzene, measuring the optical density of the solution at each stage. The results (Table 5) show that Beer's law is accurately obeyed.

TABLE 1.

Typical analyses.

BuLi (ml.)	0·1N-HCl used in titrn. (ml.)	$[Li]_{total}$ (mole $l.^{-1}$)	BuLi (ml.)	0·1N-HCl used in titrn. (ml.)	$[Li]_{total} - [BuLi]$ (mole $l.^{-1}$)
Hydrolysis with water			*Treatment with* CH_2PhCl *in* Et_2O, *then hydrolysis*		
1·82	28·2	1·55	4·90	2·42	0·049
1·44	22·5	1·567	5·91	1·98	0·034
2·25	35·15	1·563	3·85	1·50	0·039
		Av.: 1·56			Av.: 0·04

$\therefore$ $[BuLi] = 1{\cdot}56 - 0{\cdot}04 = 1{\cdot}52$ mole $l.^{-1}$.

TABLE 2.

Dependence of the initial rate of reaction on butyl-lithium concentration, at 30·5°.

$10^4[CH_2{:}CPh_2]_i$ (mole $l.^{-1}$)	$10^4[BuLi]_i$ (mole $l.^{-1}$)	R_i (D $hr.^{-1}$)	$R_i/[BuLi]_i^{0{\cdot}18}$
1·01	10·2	0·084	0·290
1·01	151	0·114	0·248
1·01	981	0·192	0·292

Extinction coefficient. Since the reaction is irreversible under the conditions used and Beer's law is obeyed, the extinction coefficient of the coloured species was found from the optical density at complete reaction. Its value is $1{\cdot}6 \pm 0{\cdot}2 \times 10^4$ at the wavelength of maximum absorption (428 mμ).

Temperature-dependence. The temperature-dependence of the initial rate of reaction at constant initial olefin and butyl-lithium concentrations is given in Table 6. The apparent activation energy, found by plotting $\log_{10} k$ against $1/T$ was $16{\cdot}4 \pm 0{\cdot}7$ kcal. mole^{-1}.

TABLE 3.

First-order dependence of reaction rate on 1,1-diphenylethylene, when butyl-lithium is in excess.

$[CH_2{:}CPh_2]_i = 1{\cdot}01 \times 10^{-4}$ mole l.$^{-1}$. $[LiBu]_i = 151 \times 10^{-4}$ mole l.$^{-1}$. $a = 1{\cdot}673$ (*i.e.*, the value of D at $t = \infty$).

Time (hr.)	Reaction (%)	D at time t ("x")	$\log_{10}\left(\frac{a}{a-x}\right)$	First-order rate constant (hr.$^{-1}$)	Time (hr.)	Reaction (%)	D at time t ("x")	$\log_{10}\left(\frac{a}{a-x}\right)$	First-order rate constant (hr.$^{-1}$)
1	6·87	0·115	0·0310	0·071	16	66·04	1·105	0·4692	0·068
2	13·45	0·225	0·0627	0·072	18	70·00	1·171	0·5228	0·066
3	19·43	0·325	0·0938	0·072	20	72·28	1·226	0·5732	0·066
4	24·99	0·418	0·1249	0·072	22	76·50	1·280	0·6291	0·066
5	30·00	0·502	0·1549	0·071	24	79·50	1·330	0·6882	0·066
6	34·66	0·580	0·1849	0·071	26	81·34	1·361	0·7392	0·066
7	38·92	0·650	0·2137	0·070	28	84·20	1·409	0·8019	0·066
8	42·62	0·713	0·2412	0·069	30	86·44	1·446	0·8675	0·067
9	46·62	0·780	0·2726	0·070	32	88·47	1·480	0·9379	0·068
10	50·02	0·837	0·3013	0·069	34	90·00	1·506	1·0008	0·068
12	56·48	0·945	0·3614	0·069	46	95·74	1·602	1·3722	0·069
14	61·67	1·032	0·4166	0·069					

TABLE 4.

$10^4[CH_2{:}CPh_2]_i$ (mole l.$^{-1}$)	$10^4[BuLi]_i$ (mole l.$^{-1}$)	R_i (D hr.$^{-1}$)	$R_i/[CH_2{:}CPh_2]_i^1[BuLi]_i^{0\cdot18}$
2·39	30·46	0·22	$2{\cdot}6 \times 10^3$
1·01	10·2	0·084	$2{\cdot}87 \times 10^3$

TABLE 5.

Test of Beer's law: dilution of a solution containing $7{\cdot}36 \times 10^{-5}$ mole l.$^{-1}$ of $Bu{\cdot}CH_2{\cdot}CPh_2^-Li^+$ at 20°.

$10^5[Bu{\cdot}CH_2{\cdot}CPh_2^-Li^+]$ (mole l.$^{-1}$)	7·36	5·61	3·77	1·95
Optical density (D)	1·18	0·90	0·60	0·271
$10^{-4}D/[Bu{\cdot}CH_2{\cdot}CPh_2^-Li^+]$	1·6	1·6	1·6	1·4

TABLE 6.

Temperature-dependence.

10^5k (mole$^{-0\cdot18}$ l.$^{0\cdot18}$ sec.$^{-1}$)	8·91	4·17	2·51	1·75	0·6
Temp. (K)	313·4°	303·5°	298·2°	293·1°	284·4°

Interaction of Butyl-lithium with 1,1,3,3-Tetraphenylbut-1-ene and Tetraphenylethylene.—When butyl-lithium was mixed with either of these substances in benzene under rigorous high-vacuum conditions, no colour developed even after several weeks at 30°. This was true both at low concentrations, comparable with those used for 1,1-diphenylethylene, and at much higher concentrations, *e.g.*, 0·26 mole l.$^{-1}$ of butyl-lithium and 0·42 mole l.$^{-1}$ of 1,1,3,3-tetraphenylbut-1-ene, and 0·035 mole l.$^{-1}$ of butyl-lithium and 0·082 mole l.$^{-1}$ of tetraphenylethylene. At these high concentrations the butene and tetraphenylethylene could be recovered unchanged from the solutions.

XUM

Discussion

Spectrum of the Solution.—Our results show that butyl-lithium reacts with 1,1-diphenylethylene to give a coloured product having the spectrum given in Fig. 4, curve A. Since Ziegler *et al.*[8] showed by analysis of the product that when butyl-lithium adds to 1,1-diphenylethylene the butyl group is attached to the primary carbon atom we attribute this spectrum to the ion pair $Bu{\cdot}CH_2{\cdot}CPh_2^-Li^+$. The wavelength of maximum absorption of this ion is the same as that for the corresponding carbonium ion [9] (Fig. 4, curve B) but the shape of the spectrum is somewhat different; it is broader and extends further into the visible region.

The extinction coefficient of the ion pair at the wavelength of maximum absorption (428 mμ) was $1{\cdot}6 \times 10^4$, slightly less than that ($2{\cdot}8 \times 10^4$) for the corresponding carbonium ion.

Mechanism of the Reaction.—We have found the order of reaction to be unity in 1,1-diphenylethylene and 0·18 in butyl-lithium.

There is much evidence that butyl-lithium is highly associated in benzene,[10] and the majority of results indicate that it is mainly present as the hexamer $(BuLi)_6$. If we assume (as was done [11] for the butyl-lithium-catalysed polymerisation of styrene in benzene) (i) that an equilibrium exists between associated and unassociated molecules of butyl-lithium which, under the conditions of our experiments lies well towards the associated side, and (ii) that only monomeric butyl-lithium reacts with 1,1-diphenylethylene, then the following reaction scheme is consistent with our results:

$$\tfrac{1}{6}(BuLi)_6 \underset{b}{\overset{a}{\rightleftharpoons}} BuLi \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$BuLi + CH_2{:}CPh_2 \longrightarrow Bu{\cdot}CH_2{\cdot}CPh_2^-Li^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The rate of production of ion pairs would be given by the expression:

Rate of production of ion pairs $= k_2[BuLi][CH_2{:}CPh_2]$, and since $[BuLi]/[(BuLi)_6]^{\frac{1}{6}} = k_{1a}/k_{1b} = K_1$, we have:

Rate of production of ion pairs $= k_2K_1[(LiBu)_6]^{\frac{1}{6}}[CH_2{:}CPh_2]$.

The order of reaction would, from this equation, be unity in 1,1-diphenylethylene and $\frac{1}{6}$ (0·167) in butyl-lithium. These values are in good agreement with those we find experimentally. Thus our velocity constant k is equal to k_2K_1.

It is interesting to compare our results for the addition of butyl-lithium to 1,1-diphenylethylene in benzene with those obtained for the addition of butyl-lithium to styrene in benzene, *i.e.*, for initiation of the polymerisation of styrene by butyl-lithium. Bywater and Worsfold [11] found that the rate of initiation varies as [Styrene] [1] and $[BuLi]^{0\cdot155}$, even down to butyl-lithium concentrations as low as 5×10^{-5} mole l.$^{-1}$. They account for this by suggesting that only monomeric butyl-lithium can initiate the polymerisation of styrene, and that within the concentration range they use the butyl-lithium is associated six-fold, the equilibrium lying heavily towards the associated form.

Welch [11] also studied the butyl-lithium-catalysed polymerisation of styrene in benzene, and concluded that above a concentration of 2×10^{-2} mole l.$^{-1}$ the butyl-lithium is six- or seven-fold associated, but that below this concentration it is monomeric. Our results agree with those of Bywater and Worsfold, and not with those of Welch, for we have observed first-order dependence on the olefin and a low order of 0·18 in butyl-lithium over a concentration range of butyl-lithium from 10^{-3} to 10^{-1} mole l.$^{-1}$ We disagree, however,

[8] Ziegler, Crossman, Kleiner, and Schafer, *Annalen*, 1929, **473**, 1.
[9] Evans, *J. Appl. Chem.*, 1951, **1**, 240.
[10] Rogers, *J. Phys. Chem.*, 1957, **61**, 366; Warhurst, *Discuss. Faraday Soc.*, 1947, **2**, 239; Coates, "Organo-Metallic Compounds," Methuen & Co., London, 1956, p. 7.
[11] Welch, *J. Amer. Chem. Soc.*, 1959, **81**, 1345; Bywater and Worsfold, *Canad. J. Chem.*, 1960, **38**, 1891.

with Ziegler *et al.*[8] who concluded that the reaction between butyl-lithium and 1,1-diphenylethylene was of the first order in olefin and in butyl-lithium for reagent concentrations of 0·15 mole l.$^{-1}$.

Temperature-dependence.—Our results show an apparent activation energy for the reaction of 16·4 kcal. mole^{-1}. Since the concentration of monomeric butyl-lithium in reaction (2) depends on equilibrium (1), this value will equal the activation energy of reaction (2) plus the endothermicity of reaction 1(*a*), *i.e.*, $\Delta H^0_{1a} + \Delta H_2^{\ddagger} = 16{\cdot}4$ kcal. mole^{-1}. Bywater and Worsfold obtained a value of 18 kcal. mole^{-1} (velocity constant = $2{\cdot}3 \times 10^{-5}$ l.$^{0{\cdot}167}$ mole$^{-0{\cdot}167}$ sec.$^{-1}$ at 30°) for the addition of butyl-lithium to styrene. Our value of 16·4 kcal. mole^{-1} (velocity constant = $4{\cdot}17 \times 10^{-5}$ l.$^{0{\cdot}18}$ mole$^{-0{\cdot}18}$ sec.$^{-1}$ at 30°) for its addition to 1,1-diphenylethylene is less than this, indicating that introduction of a second phenyl group into styrene stabilises the negative ion to a greater extent than it does the olefin.

Steric Hindrance.—No colour is obtained when butyl-lithium is mixed with the linear dimer of 1,1-diphenylethylene, $CH_3{\cdot}CPh_2{\cdot}CH{:}CPh_2$, or with tetraphenylethylene, although both these olefins give coloured carbonium ions when treated with dilute acids.[12] Courtauld's atomic models indicate that the butyl group can be added to the monomer to form $Bu{\cdot}CH_2{\cdot}CPh_2^-$, but not to the linear dimer to form $CH_3{\cdot}CPh_2{\cdot}CHBu{\cdot}CPh_2^-$, or to tetraphenylethylene to form $Bu{\cdot}CPh_2{\cdot}CPh_2^-$. We attribute the absence of colour in the last two cases to steric hindrance which prohibits the formation of the anion by addition of a butyl group.

Dimerisation.—In our preliminary communication [2] we stated that for a benzene solution containing 0·4 mole l.$^{-1}$ of butyl-lithium and 0·7 mole l.$^{-1}$ of 1,1-diphenylethylene there was no reaction of the ion pair (formed by the addition of the butyl-lithium to the olefin) with the excess of olefin. Further work, with a large excess of 1,1-diphenylethylene, seems to indicate a slow reaction of the ion pair with the excess of olefin. This is being investigated.

The fact that our optical density–time plots are of first order up to at least 96% reaction shows that for the work reported in this paper there is no appreciable dimerisation of the type: $Bu{\cdot}CH_2{\cdot}CPh_2^-Li^+ + CH_2{:}CPh_2 \longrightarrow BuCH_2{\cdot}CPh_2{\cdot}CH_2CPh_2^-Li^+$, and that this reaction, if it does occur, must be very much slower than the rate of addition of butyl-lithium.

In the case of styrene, on the other hand, the propagation reaction, $\sim CH_2{\cdot}CHPh^-Li^+ + CH_2{:}CHPh \longrightarrow \sim CH_2{\cdot}CHPh{\cdot}CH_2{\cdot}CHPh^-Li^+$, is much faster than addition of butyl-lithium; Welch [11] suggests a value of 5 and Bywater and Worsfold [11] a value of about 550 for the ratio, k(propagation) : k(initiation).

We thank the Distillers Company Limited for financial help. One of us (D. B. G.) thanks the D.S.I.R. for a Research Studentship.

UNIVERSITY COLLEGE, CARDIFF. [*Received, April 28th,* 1961.]

[12] Evans, N. Jones, and Thomas, *J.*, 1955, 1824; Evans, P. M. S. Jones, and Thomas, *J.*, 1957, 104.

911. *The Synthesis of 3-Alkyl-1-arylsulphonyl-hydantoins and -2-thiohydantoins.*

By G. Holan and E. Samuel.

N^1-Alkyl-N^2-arylsulphonyl ureas with ethyl chloroacetate give 3-alkyl-1-arylsulphonylhydantoins whose structures are confirmed by independent synthesis of a 1-arylsulphonylhydantoin, followed by alkylation at the 3-position. An N^1-aryl-N^2-arylsulphonylurea could not be cyclised.

With ethyl chloroacetate an N^1-alkyl-N^2-arylsulphonylthiourea gave a thiazolidone, the thiourea reacting in its iso-form. The desired 3-alkyl-1-arylsulphonyl-2-thiohydantoin was obtained, together with the S-alkyl derivative, by treating the 1-arylsulphonyl-2-thiohydantoin with an alkyl iodide.

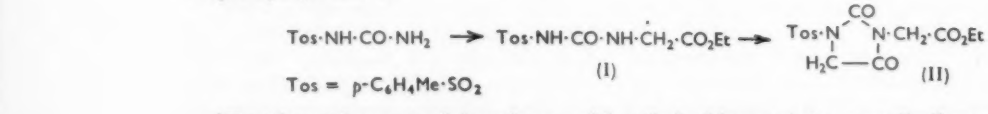
Desulphurisation of an *S*-alkyl-2-thiohydantoin with chloroacetic acid yielded the unsubstituted 1-arylsulphonylhydantoin. Sulphurisation of a 3-alkyl-1-arylsulphonylhydantoin with phosphorus pentasulphide afforded the 4-thiohydantoin.

The use of N^1-alkyl-N^2-arylsulphonylureas in oral control of diabetes is well known. In the present work we have attempted to build this structure into hydantoins and thiohydantoins, which were reported to affect the blood-sugar level of mammals.[1] The chosen compounds were the 3-alkyl-1-arylsulphonyl-hydantoins and -2-thiohydantoins.

1,3-Dialkyl(or aryl-alkyl)-hydantoins or -2-thiohydantoins are conventionally synthesized by cyclisation of an *N*-alkyl- or *N*-aryl-glycine with an alkyl isocyanate or isothiocyanate. Therefore in our work we would have required the arylsulphonyl isocyanates and isothiocyanates. Such isocyanates have been prepared,[2] but with difficulty, and their reaction with alkylglycines was accompanied by polymerization. Attempts to prepare arylsulphonyl isothiocyanates were unsuccessful.

The reverse reaction, in which an alkyl isothiocyanate was treated with an arylsulphonylglycine, afforded the arylsulphonylglycine alkylamide and the 1,4-diarylsulphonyl-2,5-dioxopiperazine, indicating that an alkyl isothiocyanate does not react with a substituted sulphonamido-group.

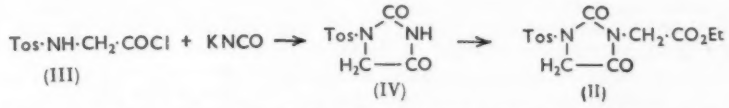
After this preliminary work the simplest approach appeared to be cyclisation of N^1-alkyl-N^2-arylsulphonylureas with ethyl chloroacetate. Aspelund[3] cyclised N^1-methyl-N^2-phenylurea with chloroacetyl chloride or ethyl chloroacetate to the 3-methyl-4-oxo-2-phenylimino-oxazolidine and 3-methyl-1-phenylhydantoin by means of sodium in ethanol. The N^2-nitrogen of the N^1-alkyl-N^2-arylsulphonylureas is more acidic than that in the dialkyl- or alkylaryl-ureas owing to the electron-withdrawing effect of the sulphonyl group; thus their condensation with ethyl chloroacetate proceeded in aqueous ethanol or, preferably, dimethylformamide in presence of potassium carbonate as a condensing agent. We thus prepared 3-butyl-1-toluene-*p*-sulphonyl- and 1-*p*-chlorobenzenesulphonyl-3-propylhydantoin, but we failed to obtain 3-phenyl-1-toluene-*p*-sulphonylhydantoin.



Treating toluene-*p*-sulphonylurea with ethyl chloroacetate gave 3-ethoxycarbonylmethyl-1-toluene-*p*-sulphonylhydantoin (II) and the urea (I), and no 1-toluene-*p*-sulphonylhydantoin was isolated. Therefore the reaction involves further condensation of the urea (I) with ethyl chloroacetate.

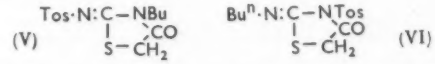
[1] Isshiki, *Pharmacol. Jap.*, 1932, **15**, No. 1, Breviaria 4.
[2] Franz, personal communication.
[3] Aspelund, *Finska Kemistsamfundets Medd.*, 1940, **49**, 49.

The hydantoin (II) was also used for the proof of the substitution pattern of the hydantoins in our reaction. This was carried out by unambiguous synthesis of the 1-toluene-*p*-sulphonylhydantoin (IV) from toluene-*p*-sulphonylglycine chloride (III) and potassium isocyanate, and conversion of this by ethyl chloroacetate into the hydantoin (II).



(III) (IV) (II)

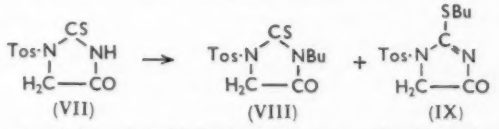
We expected that cyclisation of the N^1-alkyl-N^2-arylsulphonylthioureas with ethyl chloroacetate would yield the thiazolidones and not the 2-thiohydantoins, as thioureas generally react in their iso-form. The thiazolidone obtained by this cyclisation of N^1-butyl-N^2-toluene-*p*-sulphonylthiourea yielded on acid hydrolysis N^1-butyl-N^2-toluene-*p*-sulphonylurea, but this is not a definitive proof of structure as the same hydrolysis product would be obtained from the two isomers (V) and (VI) that could be formed in the cyclisation. Although no final proof is available, structure (V) is the more probable as the initial isomerisation of the substituted thiourea in the cyclisation would be expected to proceed by transfer of the more labile hydrogen from the sulphonamido-group to sulphur.



(V) (VI)

On failure of the chloroacetate cyclisation to yield the required 3-alkyl-1-arylsulphonyl-2-thiohydantoins several other methods of synthesis were attempted. Reaction of butyl isothiocyanate with toluene-*p*-sulphonylglycine under various conditions yielded either *N*-butyl-*N*-toluene-*p*-sulphonylacetamide or 2,5-dioxo-1,4-di-*p*-toluenesulphonylpiperazine by condensation of two molecules of the substituted glycine. On treatment of butyl isothiocyanate with the ester or acyl chloride of the arylsulphonylglycine only the starting materials were recovered. The reverse cyclisation of butylglycine with the arylsulphonyl isothiocyanate could not be carried out as attempts to prepare the isothiocyanate, or to treat it *in situ* with the butyl compound, were unsuccessful.

3-Butyl-1-toluene-*p*-sulphonyl-2-thiohydantoin (VIII) was finally prepared by reaction of 1-toluene-*p*-sulphonyl-2-thiohydantoin (VII) with butyl iodide: this gave also the *S*-alkyl derivative (IX) owing to a shift of the hydrogen from the 3-position of the thiohydantoin to sulphur. The structure of the *S*-alkyl isomer was determined by its ease of desulphurisation with chloroacetic acid to 1-toluene-*p*-sulphonylhydantoin (IV): the 3-alkylated derivative (VIII) could not be desulphurised.



(VII) (VIII) (IX)

3-Butyl-1-toluene-*p*-sulphonyl-4-thiohydantoin was obtained by sulphurisation of 3-butyl-1-toluene-*p*-sulphonylhydantoin with phosphorus pentasulphide. Elemental analysis confirmed the product as an isomer of the thiohydantoins (VIII) and (IX), its infrared spectrum was different, and mixed melting points were depressed.

Experimental

Cyclisation with Ethyl Chloroacetate.—To a stirred solution of the urea or thiourea (0·04 mole), in dimethylformamide (200 ml.), anhydrous potassium carbonate (0·04 mole) was added and the suspension heated to 80°. At this temperature ethyl chloroacetate (0·04 mole) in dimethylformamide (50 ml.) was added during 1 hr. After a further 1·5 hr. at 80° the mixture was cooled in ice, filtered, and concentrated under a vacuum. The first crop of hydantoin or

thiazolidone was filtered off. Treatment of the filtrate with dilute alkali gave a second crop. These materials were combined and recrystallised. The following were thus obtained.

3-*Butyl*-1-*toluene*-p-*sulphonylhydantoin* (35%; from *N'*-butyl-N^2-toluene-*p*-sulphonylurea [4]), needles (from ethanol), m. p. 153° (Found: C, 54·7; H, 5·9; S, 10·3. $C_{14}H_{18}N_2O_4S$ requires C, 54·2; H, 5·8; S, 10·3%).

1-p-*Chlorobenzenesulphonyl*-3-*propylhydantoin* (from N^1-*p*-chlorobenzenesulphonyl-N^2-propylurea [5]; 25%), needles (from methanol), m. p. 179° (Found: C, 45·9; H, 4·3; S, 10·0. $C_{12}H_{13}ClN_2O_4S$ requires C, 45·55; H, 4·1; S, 10·1%).

3-*Ethoxycarbonylmethyl*-1-*toluene*-p-*sulphonylhydantoin* (10%; from toluene-*p*-sulphonylurea [6]) (crystallised from methanol), m. p. 197° (Found: C, 49·3; H, 4·9; S, 9·4. $C_{14}H_{16}N_2O_6S$ requires C, 49·4; H, 4·7; S, 9·4%). Dilution with water of the dimethylformamide filtrate from the above experiment precipitated toluene-*p*-sulphonamide (80%). Acidification of the filtrate from this precipitate yielded *ethyl* **N²-*toluene*-p-*sulphonylureidoacetate*** which recrystallised from aqueous ethanol as plates (4%), m. p. 168° (Found: C, 48·3; H, 5·5; S, 11·2. $C_{12}H_{16}N_2O_5S$ requires C, 48·0; H, 5·4; S, 10·7%).

The hydantoin was also obtained from 1-toluene-*p*-sulphonylhydantoin and ethyl chloroacetate by the method used for the cyclisations.

1-*Butyl*-2-*toluene*-p-*sulphonylimino*-3-*thiazolid*-5-*one*.—This *product* (obtained by the usual cyclisation from 3-butyl-1-toluene-*p*-sulphonylthiourea [7]) formed a buff-coloured powder (from methanol) (65%), m. p. 168° (Found: C, 51·4; H, 5·5; S, 19·05. $C_{14}H_{18}N_2O_3S_2$ requires C, 51·5; H, 5·6; S, 19·05%).

1-*Toluene*-p-*sulphonylhydantoin*.—Potassium cyanate (0·12 mole) and toluene-*p*-sulphonylglycine chloride [8] (0·04 mole) were dissolved in glacial acetic acid. An exothermic reaction raised the temperature to 60°. The solution was then refluxed for 15 min. After cooling, a small amount of resin was filtered off and the filtrate was neutralised with sodium carbonate solution. The *hydantoin* precipitated was recrystallised from methanol, forming needles (5%), m. p. 226° (Found: C, 47·0; H, 4·0; S, 12·7. $C_{10}H_{10}N_2O_4S$ requires C, 47·3; H, 4·0; S, 12·6%).

1-*Toluene*-p-*sulphonylhydantoin*.—2-Butylthio-1-toluene-*p*-sulphonyl-2-imidazolin-4-one (0·01 mole) and chloroacetic acid (0·1 mole) were refluxed in water (2 ml.) for 3 hr. The precipitated 1-toluene-*p*-sulphonylhydantoin recrystallised from methanol and was identified by a mixed m. p. and its infrared spectrum.

2,5-*Dioxo*-1,4-*ditoluene*-p-*sulphonylpiperazine*.—Toluene-*p*-sulphonylglycine [9] (0·06 mole) and butyl isothiocyanate [10] (0·06 mole) were refluxed in toluene (400 ml.) with triethylamine, the water formed being removed azeotropically. After 5 hours' refluxing the toluene was evaporated. The residue, which was insoluble in both acid and alkali, recrystallised from aqueous acetone and was identified as the piperazine, m. p. 293° (lit., 225°,[11] 275° [12]) (Found: C, 51·3; H, 4·4; S, 15·1. Calc. for $C_{18}H_{18}N_2O_6S_2$: C, 51·2; H, 4·3; S, 15·2%).

N-*Butyl*-N-*toluene*-p-*sulphonamidoacetamide*.[13]—Toluene-*p*-sulphonylglycine (0·02 mole) and butyl isothiocyanate with a trace of triethylamine were heated at 100° for 10 hr. Methanol was then added and a small amount of the above dioxopiperazine was filtered off. The filtrate was diluted with water. An oil was deposited which solidified and recrystallised from aqueous ethanol and ethyl acetate–light petroleum (b. p. 40—60°). This *amide* (30%), m. p. 93° (Found: C, 55·3; H, 6·8; S, 11·4. Calc. for $C_{13}H_{20}N_2O_3S$: C, 54·9; H, 7·1; S, 11·3%), was insoluble in acid or sodium carbonate but was soluble in sodium hydroxide. Its hydrolysis products were identified as toluene-*p*-sulphonylglycine and butylamine by paper chromatography.

3-*Butyl*-1-*toluene*-p-*sulphonyl*-2-*thiohydantoin* *and* **2-*Butylthio*-1-*toluene*-p-*sulphonyl*-2-*imidazolin*-4-*one*.**—1-Toluene-*p*-sulphonyl-2-thiohydantoin (0·02 mole), potassium carbonate (0·01 mole), and butyl iodide (0·02 mole) were heated at 75—80° for 0·5 hr., then cooled and poured into water (200 ml.), and the yellow precipitate was filtered off. This was treated with hot benzene and the insoluble starting material removed. Cooling of the benzene filtrate gave

[4] Commercially available as " Orinase " or " Tolbutamide."
[5] Commercially available as " Chlorpropamide " or " Diabinese."
[6] Martin, U.S.P. 2,411,661/1946.
[7] Petersen, *Chem. Ber.*, 1950, **83**, 551.
[8] Swan, *Austral. J. Sci. Res.*, 1952, *A*, **5**, No. 4, 732.
[9] Fisher and Bergman, *Annalen*, 1913, **398**, 117.
[10] Schmidt and Schnegg, G.P. 14,755/1956.
[11] Wallin, *Acta Univ. Lundensis*, 1892, **28**, 2.
[12] Enger, *Z. physiol. Chem.*, 1930, **191**, 117.
[13] Rushig, Korger, Aumüller, Wagner, and Weyer, *Medizin und Chemie*, 1958, **6**, 61.

the S-*butyl derivative* (60%) as plates, m. p. 127° (from methanol), with an odour of butanethiol (Found: C, 51·45; H, 5·7; S, 19·5. $C_{14}H_{18}N_2O_3S_2$ requires C, 51·5; H, 5·6; S, 19·6%).

The filtrate was chromatographed on alumina, and the 3-*butylthiohydantoin* eluted with benzene and recrystallised from methanol as a yellowish powder (12%), m. p. 106° (Found: C, 51·6; H, 5·85; S, 19·6. $C_{14}H_{18}N_2O_3S_2$ requires C, 51·5; H, 5·6; S, 19·6%).

The *S*-alkyl derivative was desulphurised with chloroacetic acid to 1-toluene-*p*-sulphonylhydantoin. The 3-alkyl derivative gave toluene-*p*-sulphonylglycine on alkaline hydrolysis.

3-*Butyl*-1-*toluene*-p-*sulphonyl*-4-*thiohydantoin*.—3-Butyl-1-toluene-*p*-sulphonylhydantoin (0·07 mole) and phosphorus pentasulphide (0·05 mole) were refluxed for 1 hr. in tetralin (20 ml.). On cooling, crystals were formed which, recrystallised from methanol, gave the 4-*thiohydantoin* as white needles (20%), m. p. 167° (Found: C, 51·9; H, 5·6; S, 19·9. $C_{14}H_{18}N_2O_3S_2$ requires C, 51·5; H, 5·6; S, 19·6%).

We thank Drs. J. Bornstein and H. G. Burger of the Alfred Hospital Diabetic and Metabolic Unit for biological testing, Mr. R. W. Hinde for helpful suggestions in carrying out this work, and Professor G. M. Badger, of the University of Adelaide, for reading the manuscript.

MONSANTO CHEMICALS (AUSTRALIA) LTD.,
WEST FOOTSCRAY, W.12, VICTORIA. [*Received, May 4th*, 1961.]

---

912. *Polymerisation of Flavans. Part V.* The Stereochemistry of* 2,3-trans-*Flavan*-3,4-*diols.*

By M. M. BOKADIA, B. R. BROWN, P. L. KOLKER, C. W. LOVE, J. NEWBOULD, G. A. SOMERFIELD, and P. M. WOOD.

The *cis*- or *trans*-arrangement of the hydroxyl groups in eight 2,3-*trans*-flavan-3,4-diol racemates has been established by consideration of their isopropylidene derivatives, their rates of reaction with lead tetra-acetate, and the proton magnetic resonance spectra of their diacetates. This necessitates a revision of the existing assignment of relative stereochemistry to the two racemates of 4′-methoxy-6-methyl-2,3-*trans*-flavan-3,4-diol. The most convenient preparative method for the 2,3-*trans*-flavan-3,4-*cis*-diols makes use of the reduction of 3-hydroxy-2,3-*trans*-flavan-4-ones with a mixture of lithium aluminium hydride and aluminium chloride.

THE realisation [1] of the wide occurrence and importance of flavan-3,4-diols (leucoanthocyanidins) (I) in Nature has focused attention on the stereochemistry both of the natural diols [2] and of those produced by various synthetical routes.[3] Flavan-3,4-diol (I; R = R′ = H) can exist in eight stereoisomeric forms, which afford four racemates. The work described here is limited to 2,3-*trans*-flavan-3,4-diols obtained from 3-hydroxy-2,3-*trans*-flavan-4-ones, whose relative stereochemistry at the 2,3-positions is well established.[4,3c]

Bognár and Rákosi [3b] have shown that reduction of 2,3-*trans*-3-hydroxyflavan-4-one (II; R = R′ = H) with lithium aluminium hydride, sodium borohydride, or hydrogen over palladium–charcoal leads to a flavan-3,4-diol of m. p. 145—146°. Examination of the crude products from these reductions by chromatography on thin silica films [5] has shown that they contain 3-hydroxyflavanone and its oxidation product, 3-hydroxyflavone,

* Part IV, *J.*, 1961, 3677.

[1] *E.g.*, Bate-Smith and Swain, *Chem. and Ind.*, 1953, 377; King and Bottomley, *J.*, 1954, 1399; Keppler, *J.*, 1957, 2721.

[2] *E.g.*, King and Clark-Lewis, *J.*, 1955, 3384; Weinges, *Annalen*, 1959, **627**, 229; Clark-Lewis and Roux, *J.*, 1959, 1402; Clark-Lewis and Mortimer, *J.*, 1960, 4106; Clark-Lewis and Katekar, *Proc. Chem. Soc.*, 1960, 345.

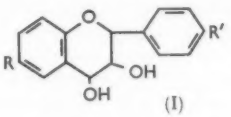
[3] *E.g.*, (*a*) Kulkarni and Joshi, *Chem. and Ind.*, 1954, 1421; *J. Indian Chem. Soc.*, 1957, **34**, 753; (*b*) Bognár and Rákosi, *Acta Chim. Acad. Sci. Hung.*, 1958, **14**, 369; (*c*) Bognár, Rákosi, Fletcher, Philbin, and Wheeler, *Tetrahedron Letters*, 1959, No. 19, 4.

[4] Mahesh and Seshadri, *Proc. Indian Acad. Sci.*, 1955, **41**, 210.

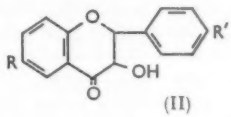
[5] Stahl, *Arch. Pharm.*, 1959, **292**, 411.

XUM

which are easily removed by recrystallisation and chromatography on alumina to yield the pure diol of m. p. 146°. This diol yields a diacetate of m. p. 92—93·5°; Bognár and Rákosi [3b] could only obtain this diacetate as an oil. It has already been reported [6] that this diol is cleaved by lead tetra-acetate to yield a dihydrobenzofuran aldehyde which can



(I)



(II)

be converted into 2-phenylbenzofuran and that this may be regarded as a diagnostic reaction for flavan-3,4-diols.

Reduction of 3-hydroxyflavanone with a mixture of lithium aluminium hydride and aluminium chloride [7] yields another flavan-3,4-diol, of m. p. 162—163°, which has been shown to be identical with that obtained by the method of Bognár *et al.*[3c] from 3-hydroxyflavanone oxime through 4-aminoflavan-3-ol. The preparation using the mixed reagent is the more convenient. Since it is known that aluminium chloride, in these mixed reductions, is capable of causing rearrangements [8] and also that rearrangements can occur in the treatment of amines with nitrous acid,[9] this compound of m. p. 162—163° has been cleaved with lead tetra-acetate and 2-phenylbenzofuran has been isolated, which establishes the flavan-3,4-diol structure of this compound.[6]

The diol of m. p. 162—163° yields, with ethyl chloroformate, a cyclic carbonate, m. p. 134·5—135°; the diol of m. p. 146° yields a different cyclic carbonate, m. p. 129—130·5°; so, contrary to the assumption of Kulkarni and Joshi,[3a] the formation of a cyclic carbonate cannot be taken as evidence for a *cis*-diol.[10] However, the diol of m. p. 162—163° yields an isopropylidene derivative in 69% yield, whereas the diol of m. p. 146° yields 10% of the same isopropylidene derivative under identical conditions. Hydrolysis of this derivative with aqueous acid gives the diol of m. p. 162—163°. From these observations, the conclusion is drawn that the diol of m. p. 162—163° is a *cis*-diol, *i.e.*, 2,3-*trans*-flavan-3,4-*cis*-diol and that the diol of m. p. 146° is a *trans*-diol, *i.e.*, 2,3-*trans*-flavan-3,4-*trans*-diol. The conclusions of H. C. Brown [11] about the stability of five-membered rings and the observations of Angyal and Macdonald [10] on the formation of carbonates make it not unexpected that only the *cis*-diol forms an isopropylidene derivative, but that the *cis*- and *trans*-diols form distinct cyclic carbonates.

The diol of m. p. 162—163° reacts with lead tetra-acetate approximately five times as fast as does the diol of m. p. 146°. Comparison with values in the literature [12] for known *cis*- and *trans*-diols confirms the above assignment of stereochemistry.

Finally, these conclusions have been confirmed by an examination of the proton magnetic resonance spectra of the diacetates of the two diols in chloroform. The acetoxy-group in these compounds shows a sharp proton resonance peak unsplit by spin–spin coupling. Similar single peaks have been found in the proton resonance spectra of some acetylated pyranose sugars.[13] In these it has been found that peaks for axial acetoxy-groups always occur at a lower field than those for equatorial acetoxy-groups, *i.e.*, $\tau_{ax.}$ 7·97—8·13 and $\tau_{eq.}$ 8·13—8·31. On this basis, the acetoxy-group proton resonance peaks from the flavan-3,4-diol diacetates have been assigned. Since only relative values of chemical shifts for axial and equatorial acetoxy-groups are required, the diamagnetic

[6] Bokadia, Brown, and Cummings, *J.*, 1960, 3308.
[7] Brown, *J.*, 1952, 2756; Brown and White, *J.*, 1957, 3755.
[8] Clark-Lewis, *J.*, 1960, 2433; Brown, Trown, and Woodhouse, *J.*, 1961, 2478.
[9] Henry, *Compt. rend.*, 1907, **145**, 899, 1247.
[10] Angyal and Macdonald, *J.*, 1952, 686.
[11] Brown, *J.*, 1956, 1248.
[12] Criegee, *Ber.*, 1932, **65**, 1770; 1940, **73**, 563, 571; *Sitzungsber. Ges. Naturwiss. Marburg*, 1934, **69**, 26; Criegee, Kraft, and Rank, *Annalen*, 1933, **507**, 159.
[13] Lemieux, Kullnig, and Moir, *J. Amer. Chem. Soc.*, 1958, **80**, 2237.

anisotropy effect from the aromatic rings is not thought to be important here. Further, the configurations assigned in what follows agree with those deduced from kinetic and chemical results. Now, the diol diacetates differ in the stereochemistry of the heterocyclic ring. In each of their proton magnetic resonance spectra one peak (τ 8·16) lies in the range of chemical shifts found for equatorial acetoxy-groups in pyranose sugars. Hence, in each diol diacetate, there is an equatorial acetoxy-group. The conformation at the 2-position is expected to be the same in the two compounds and hence the difference between them depends on the conformation of the second acetoxy-group. For the diacetate of the diol of m. p. 146°, the peak of the second acetoxy-group lies at a higher field (τ 8·02) than that of the second acetoxy-group of the other diacetate (τ 7·87), and hence the former is thought to be equatorial. The second acetoxy-group in the isomer is therefore axial. This leads to the same conclusions as were drawn above, *viz.*, that the diol of m. p. 162—163° is a 3,4-*cis*-diol and the diol of m. p. 146° is a 3,4-*trans*-diol.

If we assume that the 2-aryl group in each diacetate is equatorial, it follows that, since the diols are 2,3-*trans*, the 3-acetoxy-group in each diacetate is truly equatorial (τ 8·16). The occurrence of the peak for the 4-acetoxy-group at a lower field than for acetylated pyranose sugars is probably a result of the quasi-equatorial (τ 8·02) and quasi-axial (τ 7·87) nature [14] of the 4-acetoxy-groups.

The two 6-methyl-2,3-*trans*-flavan-3,4-diols (I; R = Me, R′ = H) and the two 4′-methoxy-2,3-*trans*-flavan-3,4-diols (I; R = H, R′ = OMe), prepared from the corresponding 3-hydroxyflavanones, follow the same pattern as the two unsubstituted diols, leading to assignments of stereochemistry shown in the Table.

2,3-*trans*-Flavan-3,4-diols (I) prepared from hydroxyflavanones (II).

R	R′	Reagent	M. p.	Carbonate, m. p.	Isopropylidene deriv., m. p.	$Pb(OAc)_4$, k at 20°	Stereochem. at pos. 3,4
H	H	1 or 2 [3c]	162—163°	134·5—135°	113—114° (69%)	0·20	*cis*
		3 [3b] or 4 [3b]	146—146·5	129—130·5	112·5—113·5† (10%)	0·036	*trans*
Me	H	1	178—179	173—174	91·5—92·5 (58%)	0·24	*cis*
		3	118—119	159·5—161	91—92 † (10%)	0·079	*trans*
H	MeO	1	160—161	185·5—187	110—110·5 (69%)	0·29	*cis*
		3	177—177·5	190—191	—	0·039	*trans*
Me	MeO	1 or 2 [3c]	192·5—194	167—168	129—130 (70%)	0·43	*cis*
		3 [3a] or 5 [3a]	172—173	136—137·5	129—130 † (71%)	0·063	*trans*

* Reagents: 1, $LiAlH_4$–$AlCl_3$. 2, Through oxime. 3, $LiAlH_4$. 4, H_2–Pd. 5, H_2–Pt–AcOH.
† Deriv. of *cis*-diol.

The two diols obtained by Kulkarni and Joshi [3c] from 3-hydroxy-4′-methoxy-6-methylflavanone (II; R = Me, R′ = OMe) have been re-examined. Reduction of the hydroxyflavanone with lithium aluminium hydride yields the diol of m. p. 172—173° in greater amount, and reduction with the mixed reagent gives the diol of m. p. 192·5—194°. By analogy with the diols previously discussed, it can be inferred, from the methods of preparation alone, that these are the *trans*- and the *cis*-diol respectively, and this conclusion is confirmed by consideration of the cyclic derivatives of the diols and of their rates of reaction with lead tetra-acetate (see the Table). Further, the proton magnetic resonance spectra of the diol diacetates are, on this basis, analogous to those of the diacetates of the unsubstituted diols described above. The assignments are contrary to those made by Kulkarni and Joshi [3c] on the basis of the formation of a cyclic carbonate by the lower-melting diol and of conformational analysis.

Experimental

Light petroleum refers to the fraction of b. p. 60—80°. Alumina was Spence's grade H deactivated with acetic acid. Infrared spectra were measured for Nujol mulls on a Perkin-Elmer model 21 spectrometer.

[14] Philbin and Wheeler, *Proc. Chem. Soc.*, 1958, 167.

2,3-trans-*Flavan*-3,4-cis-*diol*.—(i) *Preparation.* 3-Hydroxyflavanone (1·00 g.) in tetrahydrofuran (35 ml.) was added at room temperature to a solution of lithium aluminium hydride (0·30 g.) and aluminium chloride (2·10 g.) in tetrahydrofuran (40 ml.). The mixture was boiled for 1·5 hr. Decomposition with methyl formate and dilute acid and extraction with ether gave the diol, which separated from methanol as prisms (0·60 g.), melting at 162—163° with progressive sublimation and change of crystalline form to needles (Found: C, 74·6; H, 5·64. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·8%), $\nu_{max.}$ 3378, 3268 (OH), 798, 758, 703 cm.$^{-1}$ (aromatic). The m. p. was unchanged on admixture with a specimen prepared by the method of Bognár *et al.*,[3c] and the infrared and ultraviolet spectra of the two specimens were identical. Chromatography in ethyl acetate–light petroleum (1 : 1 v/v) on glass plates coated with silica[5] showed the presence of one compound (brown spot after being sprayed with antimony trichloride and heated at 105° for 20 min., R_F 0·24).

(ii) *Reaction with lead tetra-acetate.* By the method previously reported[6] this diol (500 mg.) yielded benzaldehyde 2,4-dinitrophenylhydrazone (15 mg.), m. p. and mixed m. p. 237°, salicylaldehyde 2,4-dinitrophenylhydrazone (13 mg.), m. p. and mixed m. p. 252°, and the oxime (400 mg.), m. p. 170—171°, of 2-formyl-2,3-dihydro-3-hydroxy-2-phenylbenzofuran. Treatment of the oxime with hot dilute sulphuric acid gave 2-phenylbenzofuran, m. p. and mixed m. p. 120—121·5°, identical in infrared and ultraviolet spectra with authentic material.

This reaction had $k = 0{\cdot}20$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 20·0°.

The general method of determining such rate constants was as follows.[15] Lead tetra-acetate was recrystallised from acetic acid. Acetic acid was purified by the method of Eichelberger and LaMer.[16] Water was twice distilled from potassium permanganate in an all-glass apparatus. A thermostat bath was used whose temperature was controlled within $\pm 0{\cdot}05°$. The reactions were performed in a standard 50-ml. flask. The diols used were analytically pure specimens. The diol (*ca.* $2{\cdot}5 \times 10^{-4}$ mole) was weighed into the reaction vessel, and acetic acid (37·5 ml.) containing 10 moles % of water was added. The vessel was left in the thermostat bath for several hours to attain a constant temperature. A solution (12·5 ml.) of lead tetra-acetate ($2{\cdot}5$—$3{\cdot}0 \times 10^{-2}$M) in acetic acid (containing 10 moles % of water), also kept in the thermostat bath for several hours, was added and the flask was shaken. 5-Ml. aliquot parts were withdrawn at determined times and added to *ca.* 5 ml. of stopping solution [potassium iodide (100 g.) and sodium acetate (500 g.) in water (1 l.)]. The iodine liberated was titrated against 0·005N-sodium thiosulphate (starch indicator). The original strength of the solution of lead tetra-acetate was also estimated. The rate constants were calculated in the usual way from straight-line plots of $\log_{10} a(b - x)/b(a - x)$ against time.

(iii) The *diacetate*, prepared in the usual way by using pyridine and acetic anhydride, separated from light petroleum as prisms, m. p. 97—98° (Found: C, 70·0; H, 5·4. $C_{19}H_{18}O_5$ requires C, 69·95; H, 5·5%). Hydrolysis of the diacetate (100 mg.) with a boiling mixture of 40% aqueous sodium hydroxide (1 ml.) and ethanol (4 ml.) or reduction with lithium aluminium hydride in ether gave 2,3-*trans*-flavan-3,4-*cis*-diol (60 mg.), m. p. and mixed m. p. 162—163°.

This diacetate in chloroform gave $\tau = 7{\cdot}87$ (axial OAc) and 8·16 (equatorial OAc).

In general, proton magnetic resonance spectra were recorded at 29·913 mc./sec. on a high-resolution spectrometer described previously.[17] Chemical shifts were measured relative to tetramethylsilane as an internal standard and are quoted as τ values.[18] The instrument was adjusted to repeat the recordings of each spectrum five times, and the base line was calibrated by the conventional side-band technique. The compounds were dissolved in chloroform which had been washed twice with concentrated sulphuric acid and three times with water, followed by distillation.

(iv) *Carbonate.* The diol (100 mg.) in benzene (6 ml.), ethyl chloroformate (1 ml.), and dioxan (1 ml.) was treated with triethylamine (1 ml.) and kept at room temperature overnight. Filtration, removal of the solvent, and crystallisation of the residue from light petroleum gave 2,3-trans-*flavan*-3,4-cis-*diol carbonate* (65 mg.), m. p. 134·5—135° (Found: C, 71·7; H, 4·45. $C_{16}H_{12}O_4$ requires C, 71·65; H, 4·5%), $\nu_{max.}$ 1815 and 1797 cm.$^{-1}$ (cyclic carbonate).[19] Bognár *et al.*[3c] report m. p. 159° for a carbonate prepared by the action of carbonyl chloride on the diol.

[15] Cordner and Pausacker, *J.*, 1953, 102.
[16] Eichelberger and LaMer, *J. Amer. Chem. Soc.*, 1933, **55**, 3633.
[17] Leane, Richards, and Schaefer, *J. Sci. Instr.*, 1959, **36**, 230.
[18] Tiers, *J. Phys. Chem.*, 1958, **62**, 1151.
[19] Angell, *Trans. Faraday Soc.*, 1956, **52**, 1178.

(v) *Isopropylidene derivative.* The diol (100 mg.) was shaken with anhydrous copper sulphate (1·00 g.) in acetone (30 ml.) for 8 days at room temperature. Filtration, removal of the solvent, and crystallisation from methanol gave the isopropylidene derivative (80 mg.) as needles, m. p. 112·5—113·5° (Found: C, 76·6, 77·0, 76·2; H, 6·6, 6·6, 6·2. Calc. for $C_{18}H_{18}O_3$: C, 76·6; H, 6·4%), $\nu_{max.}$ 884 cm.$^{-1}$ (CMe_2O_2;[20] not present in original diol). Bognár *et al.*[3c] report m. p. 110—111°.

2,3-trans-*Flavan*-3,4-trans-*diol.*—(i) *Preparation.* The methods described by Bognár and Rákosi[3b] gave crude material, m. p. 135—141°. Chromatography on silica films in ethyl acetate–light petroleum (1 : 1 v/v) showed the presence of 3-hydroxyflavone (yellow fluorescent spot in ultraviolet light, yellow in daylight, R_F 0·55), 3-hydroxyflavanone (white fluorescent spot in ultraviolet light, R_F 0·49), and flavan-3,4-diol (brown spot with antimony trichloride, R_F 0·24). Recrystallisation from aqueous methanol gave needles, m. p. 139—142°, which contained 3-hydroxyflavanone and flavan-3,4-diol. Chromatography of this mixture (1·20 g.) on alumina (15% deactivated; 30 g.) and elution with ether (50 ml.) gave 3-hydroxyflavanone (0·086 g.) which separated from benzene as needles, m. p. and mixed m. p. 178—180°. Further elution with ether (150 ml.) gave 2,3-*trans*-flavan-3,4-*trans*-diol (0·86 g.), needles (from methanol), m. p. 146—146·5° (Found: C, 74·1; H, 5·85. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·8%), $\nu_{max.}$ 3260 (OH), 755, 698 cm.$^{-1}$ (aromatic), R_F 0·24 on a silica film (one spot, brown, antimony trichloride).

(ii) *Rate of reaction with lead tetra-acetate.* This reaction had k 0·036 mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 20·0°.

(iii) The *diacetate* separated from light petroleum as prisms, m. p. 92—93·5° (Found: C, 70·1; H, 5·4. $C_{19}H_{18}O_5$ requires C, 69·95; H, 5·5%). Hydrolysis of the diacetate (100 mg.) with a boiling mixture of 40% aqueous hydroxide (1 ml.) and ethanol (4 ml.) gave 2,3-*trans*-flavan-3,4-*trans*-diol (60 mg.), m. p. and mixed m. p. 146—147°.

The diacetate in chloroform gave τ 8·02 and 8·16 (equatorial acetoxy-groups).

(iv) *Carbonate.* By the method described above for the *cis*-diol the 3,4-*trans*-diol (100 mg.) gave the *carbonate* (60 mg.) as needles, m. p. 129—130·5°, from hexane (Found: C, 71·9; H, 4·55. $C_{16}H_{12}O_4$ requires C, 71·65; H, 4·45%), $\nu_{max.}$ 1845 and 1818 cm.$^{-1}$ (cyclic carbonate). The mixed m. p. of this carbonate with that from the *cis*-diol was 100—112°.

(v) The 3,4-*trans*-diol (100 mg.) was treated with copper sulphate and acetone as described above. The product was an oil whose infrared spectrum showed the presence of 3-hydroxyflavanone. Chromatography on silica films showed the presence of four compounds with R_F 0·26, 0·54, 0·49, and 0·60 (pink spot with antimony trichloride) corresponding respectively to markers of flavan-3,4-diol, 3-hydroxyflavone, 3-hydroxyflavanone, and the isopropylidene derivative of the 3,4-*cis*-diol. Several recrystallisations of the oil from acetone–water (2 : 1 v/v) gave a solid which was chromatographed on alumina in benzene and recrystallised from methanol to yield the isopropylidene derivative of 2,3-*trans*-flavan-3,4-*cis*-diol (12 mg.) as needles, m. p. and mixed m. p. 113—114°, hydrolysed by dilute acid to the *cis*-diol.

6-*Methyl*-2,3-trans-*flavan*-3,4-cis-*diol.*—(i) 3-*Hydroxy*-6-*methyl*-2,3-trans-*flavan*-4-*one.* 2′-Hydroxy-5′-methylchalcone (3·80 g.) in fine suspension in ethanol (30 ml.) was treated with a mixture of aqueous hydrogen peroxide (30% v/v) (4·80 ml.) and 2N-sodium hydroxide (3·90 ml.) in one portion. After 4 hr. at 30° with occasional shaking, the mixture was acidified (60 ml. of 1·7% aqueous sulphuric acid), and the precipitate was separated, washed with water, and crystallised from methanol (50 ml.), to give yellow needles (0·10 g.) of 3-hydroxy-6-methylflavone, m. p. 201—202°. Auwers and Müller[21] give m. p. 196—197°. Evaporation of the mother liquor and two recrystallisations of the residue from benzene gave 3-*hydroxy*-6-*methyl*-2,3-trans-*flavan*-4-*one* as needles (1·50 g.), m. p. 147—149° (Found: C, 75·3; H, 5·7. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%), $\nu_{max.}$ (in EtOH) 216·5, 254, and 329 mμ (log ε 4·51, 3·94, and 3·52), $\nu_{max.}$ 3420 (OH) and 1692 cm.$^{-1}$ (C=O).

(ii) (a) 6-*Methyl*-2,3-trans-*flavan*-3,4-cis-*diol.* The above flavanone (1·00 g.) was reduced in the usual way with lithium aluminium hydride (0·30 g.) and aluminium chloride (2·30 g.) in tetrahydrofuran (40 ml.). Recrystallisation of the product from methanol gave the 3,4-cis-*diol* (0·75 g.) as needles, m. p. 178—179° (Found: C, 75·4; H, 6·3. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·25%), $\nu_{max.}$ 3230, 3510 (infl.) (OH), 825, 817, 774, 753, 698, and 688 cm.$^{-1}$ (aromatic).

[20] Ginsburg, *J. Amer. Chem. Soc.*, 1953, **75**, 5746.
[21] Auwers and Müller, *Ber.*, 1908, **41**, 4239.

Its reaction with lead tetra-acetate had $k = 0{\cdot}24$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 19·9°.

(b) The *carbonate*, prepared in the usual way, separated from benzene–light petroleum (1 : 2 v/v) as needles, m. p. 173—174° (Found: C, 72·45; H, 5·15. $C_{17}H_{14}O_4$ requires C, 72·35; H, 5·0%), $\nu_{max.}$ 1818 and 1792 (infl.) cm.$^{-1}$ (cyclic carbonate).

(c) *Isopropylidene derivative*. The diol (80 mg.) with acetone and copper sulphate gave an oil which yielded a solid (40 mg.) on crystallisation from aqueous methanol. Recrystallisation from methanol gave the *isopropylidene derivative* as needles, m. p. 91·5—92·5° (Found: C, 76·65; H, 6·8. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%), $\nu_{max.}$ 884 cm.$^{-1}$ (CMe_2O_2). Evaporation of the mother liquors gave an oil which was chromatographed on alumina (10% deactivated; 10 g.); elution with benzene (20 ml.) gave an oil (8 mg.) which was discarded; elution with ether (30 ml.) gave the unchanged diol (20 mg.), m. p. and mixed m. p. 178—179°.

6-*Methyl*-2,3-trans-*flavan*-3,4-trans-*diol*.—(i) *Preparation*. 3-Hydroxy-6-methylflavanone (1·00 g.) on reduction with lithium aluminium hydride gave the 3,4-trans-*diol* (0·80 g.) which separated from methanol as needles, m. p. 118—119° (Found: C, 75·4; H, 5·95%), $\nu_{max.}$ 3230 (OH), 864, 822, 773, 752, and 698 cm.$^{-1}$ (aromatic).

Its reaction with lead tetra-acetate had $k = 0{\cdot}079$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 19·9°.

(ii) The *diacetate* separated from light petroleum as prisms, m. p. 106—107° (Found: C, 70·5; H, 6·1%).

(iii) The *carbonate* separated from benzene–hexane as needles, m. p. 159·5—161° (Found: C, 72·6; H, 5·1%), $\nu_{max.}$ 1828 and 1795 cm.$^{-1}$ (cyclic carbonate).

(iv) Treatment of the diol (80 mg.) with acetone and copper sulphate gave an oil which on several recrystallisations from methanol gave the isopropylidene derivative of the 3,4-*cis*-diol (9 mg.) as needles, m. p. and mixed m. p. 91—92°.

4′-*Methoxy*-2,3-trans-*flavan*-3,4-cis-*diol*.—(i) *Preparation*. Reduction of 3-hydroxy-4′-methoxy-2,3-*trans*-flavan-4-one (1·35 g.) with lithium aluminium hydride and aluminium chloride in tetrahydrofuran yielded the 3,4-cis-*diol* (0·97 g.) as needles (from methanol), m. p. 160—161° (Found: C, 70·85; H, 6·4. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

(ii) *Reaction with lead tetra-acetate*. Treatment of the diol (500 mg.) in the usual way gave 2-*p*-methoxyphenylbenzofuran [6] (156 mg.) as plates, m. p. and mixed m. p. 150—151°, identical in infrared and ultraviolet spectra with authentic material.

This reaction had $k = 0{\cdot}29$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 20·0°.

(iii) The *diacetate* separated from ethyl acetate–light petroleum as prisms, m. p. 100—102° (Found: C, 67·0; H, 5·5; Ac, 24·05. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6; 2Ac, 24·15%).

(iv) The *carbonate* separated from benzene–hexane (1 : 2 v/v) as needles, m. p. 185·5—187° (Found: C, 68·45; H, 4·8. $C_{17}H_{14}O_5$ requires C, 68·45; H, 4·7%), $\nu_{max.}$ 1800 and 1772 cm.$^{-1}$ (cyclic carbonate).

(v) Prepared in the usual way by treatment of the diol (100 mg.) with acetone and copper sulphate, the *isopropylidene derivative* separated from methanol as needles (79 mg.), m. p. 110—110·5° (Found: C, 72·7, 73·05; H, 6·3, 6·6. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4%), $\nu_{max.}$ 878 cm.$^{-1}$ (CMe_2O_2).

4′-*Methoxy*-2,3-trans-*flavan*-3,4-trans-*diol*.—(i) *Preparation*.[6] The crude diol was obtained as needles, m. p. 172—176°. Examination on a silica film in ethyl acetate–light petroleum (1 : 1 v/v) showed the presence of 3-hydroxy-4′-methoxyflavanone (white fluorescent spot in ultraviolet light, R_F 0·43) and the 3,4-*trans*-diol (brown spot with antimony trichloride, R_F 0·20). Several recrystallisations from aqueous methanol (50% v/v) and finally one from methanol gave the diol as needles, m. p. 177—177·5° (Found: C, 70·5; H, 5·7%). Examination on a silica film showed one spot (brown, antimony trichloride) of R_F 0·20.

Its reaction with lead tetra-acetate had $k = 0{\cdot}039$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 20·0°.

(ii) The *diacetate* separated from light petroleum as plates, m. p. 92—93° (Found: C, 67·4; H, 5·8; Ac, 24·25, 23·85%).

(iii) The *carbonate* separated from hexane as needles, m. p. 190—191° (Found: C, 68·85; H, 4·95%), $\nu_{max.}$ 1842 and 1810 cm.$^{-1}$ (cyclic carbonate).

Treatment of the diol (100 mg.) with acetone and copper sulphate in the usual way gave the unchanged diol (90 mg.), m. p. and mixed m. p. 177—178°.

4'-Methoxy-6-methyl-2,3-trans-flavan-3,4-cis-diol.—(i) *Preparation.* 3-Hydroxy-4'-methoxy-6-methyl-2,3-*trans*-flavan-4-one (1·00 g.) was reduced in the usual way with lithium aluminium hydride (0·30 g.) and aluminium chloride (2·10 g.) in tetrahydrofuran (75 ml.). Crystallisation of the product from tetrahydrofuran gave the 3,4-*cis*-diol (0·585 g.) as needles, m. p. 192·5—194° (Found: C, 71·1; H, 6·45. Calc. for $C_{17}H_{18}O_4$: C, 71·3; H, 6·3%). Kulkarni and Joshi [3a] and Bognár *et al.*[3c] record m. p. 193°. Its reaction with lead tetra-acetate had $k = 0·43$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 19·9°.

(ii) The diacetate separated from light petroleum as prisms, m. p. 97—98° (Found: C, 68·0; H, 6·1. Calc. for $C_{21}H_{22}O_6$: C, 68·1; H, 6·0%). Kulkarni and Joshi [3a] record m. p. 98°. This diacetate in chloroform gave $\tau = 7·84$ (axial OAc) and 8·14 (equatorial OAc).

(iii) The *carbonate* separated from light petroleum–benzene (1 : 2 v/v) as needles, m. p. 167—168° (Found: C, 69·25; H, 4·8. $C_{18}H_{16}O_5$; requires C, 69·25; H, 5·1%), $\nu_{max.}$ 1797 cm.$^{-1}$ (cyclic carbonate).

(iv) The diol (90 mg.) with acetone and copper sulphate gave, in the usual way, a solid isopropylidene derivative (86 mg.) which separated from methanol as needles (62 mg.), m. p. 129—130° (Found: C, 73·75; H, 6·85. Calc. for $C_{20}H_{22}O_4$: C, 73·6; H, 6·75%). Bognár *et al.*[3c] give m. p. 126—127°. The mother-liquors afforded only unchanged diol (12 mg.), m. p. and mixed m. p. 191—193°.

4'-Methoxy-6-methyl-2,3-trans-flavan-3,4-trans-diol.—(i) *Preparation.* 3-Hydroxy-4'-methoxy-6-methyl-2,3-*trans*-flavan-4-one (2·30 g.) was reduced with lithium aluminium hydride (0·70 g.) in boiling ether (60 ml.). Crystallisation of the product from ether gave the 3,4-*trans*-diol (1·90 g.) as needles, m. p. 169—170°. Recrystallisation from methanol raised the m. p. to 172—173° (Found: C, 71·2; H, 6·4%). Kulkarni and Joshi [3a] give m. p. 169°.

Its reaction with lead tetra-acetate had $k = 0·063$ mole^{-1} l. sec.$^{-1}$ in acetic acid containing 10 moles % of water at 19·9°.

(ii) The diacetate separated from light petroleum as prisms, m. p. 121—123° (Found: C, 67·9; H, 6·0%). Kulkarni and Joshi [3a] give m. p. 123°. This diacetate in chloroform gave $\tau = 7·97$ and 8·17 (equatorial OAc).

(iii) The *carbonate* separated from light petroleum as needles, m. p. 136—137·5° (Found: C, 69·1; H, 5·1. $C_{18}H_{16}O_5$ requires C, 69·25; H, 5·1%), $\nu_{max.}$ 1826 and 1805 cm.$^{-1}$ (cyclic carbonate).

(iv) The 3,4-*trans*-diol (100 mg.) with acetone and copper sulphate gave a yellow solid (97 mg.) which on crystallisation from methanol yielded the isopropylidene derivative of the 3,4-*cis*-diol as needles (73 mg.), m. p. and mixed m. p. 129—130°. Hydrolysis of the isopropylidene derivative (15 mg.) with 2N-sulphuric acid (1 ml.) in ethanol (10 ml.) gave the 3,4-*cis*-diol (10 mg.), m. p. and mixed m. p. 191—193°.

Dyson Perrins Laboratory and Physical Chemistry Laboratory,
Oxford University.
[*Received, May 25th*, 1961.]

NOTES.

913. *Organic Fluorine Compounds. Part XXVI.* Synthesis of α-Fluoro-β-alanine.*

By Ernst D. Bergmann and Sasson Cohen.

α-Fluoro-β-alanine (I) was isolated by Heidelberger [1] as a metabolic product of 5-fluorouracil. Its potential value as an antimetabolite of β-alanine and its derivatives made a synthesis of this amino-acid desirable. The synthesis was to be based on the hydroxymethylation of ethyl fluoroacetate or a congener of this substance, after it had been shown [2,3] that ethyl fluoro-oxaloacetate condenses easily with formaldehyde. Ethyl

* Part XXV, *J.*, 1961, 4033.

[1] Heidelberger, *J. Biol. Chem.*, 1960, **235**, 433.
[2] Gault, Rouge, and Gordon, *Compt. rend.*, 1960, **250**, 1073.
[3] Bergmann and Shahak, *J.*, 1960, 5261.

αγ-difluoroacetoacetate, ethyl γγ-dichloro-α-fluoroacetoacetate, diethyl fluoromalonate and, with exceptional ease, fluoromalondiamide condense similarly with formaldehyde to give the compounds (II; R = CH_2F, R′ = OEt, R = $CHCl_2$, R′ = OEt, R = R′ = OEt

(I) $NH_2{\cdot}CH_2{\cdot}CHF{\cdot}CO_2H$ (II) $R{\cdot}CO{\cdot}CF(CH_2{\cdot}OH){\cdot}COR'$ (III) $HO{\cdot}CH_2{\cdot}CHF{\cdot}CO_2Et$

(IV) $CH_2{:}CF{\cdot}CO_2Et$ (V) $p\text{-}C_6H_4(CO)_2N{\cdot}CH_2{\cdot}CF(CO_2Et)_2$

and R = R′ = NH_2). Alkaline cleavage of the ester (II; R = $CHCl_2$, R′ = OEt) gave the expected ethyl α-fluoro-β-hydroxypropionate (III) which was converted, without isolation, into its methanesulphonate. However, reaction of the latter with potassiophthalimide in dimethylformamide only decomposed the methanesulphonate to ethyl α-fluoroacrylate (IV). On the other hand, reaction of potassiophthalimide with the methanesulphonate from the hydroxymethyl derivative (II; R = R′ = OEt) proceeded normally; hydrolysis of the product (V) with hydrochloric acid gave the desired amino-acid (I) in the form of its hydrochloride. Chromatography showed that the acid was homogeneous and that its R_F values in two solvent systems were identical with those found for Heidelberger's product.[1] A sample was kindly put at the disposal of Dr. Th. Winnick (Weizmann Institute of Science) by Dr. C. Heidelberger. We are indebted to Dr. Th. Winnick for the chromatographic identification.

Experimental.—Ethyl γγ-dichloro-α-fluoroacetoacetate. To a stirred suspension of sodium hydride (12 g.) in anhydrous ether (350 ml.) a mixture of ethyl fluoroacetate (53 g.) and ethyl dichloroacetate (109 g.) was added dropwise at such a rate that the mixture refluxed gently. Heating was continued on a water-bath for 4 hr.; then the mixture was cooled and poured on sulphuric acid (50 g.) and ice. The ethereal layer was separated and the aqueous phase extracted twice with ether. The combined ether extracts were washed with sodium hydrogen carbonate solution, dried (Na_2SO_4), and distilled. The *product* (64 g., 59%) distilled at 75—80°/0·2 mm. and had n_D^{26} 1·4555 (Found: C, 33·3; H, 3·3; F, 8·7. $C_6H_7Cl_2FO_2$ requires C, 33·2; H, 3·2; F, 8·7%).

Fluoromalondiamide. The following recipe is based on previous [4] observations. Ethyl chloroformate (217 g.) was added, dropwise and with stirring, to a cooled suspension of the sodio-enolate of ethyl fluoroacetate [from the ester (212 g.) and sodium hydride (48 g.)] in ether (1 l.), and the mixture was refluxed for 5 hr. After addition of water, the ether layer was separated and the aqueous phase extracted twice with ether. Distillation of the combined ethereal solutions permitted the recovery of unchanged ethyl fluoroacetate (80 g., 38%). The oily residue (ethyl fluoromalonate and fluoro-fluoroacetylmalonate) was added, at 5—10°, to a stirred aqueous 28% ammonia solution (500 ml.). After 21 hr. at the same temperature, the precipitate (50 g., 21%, or 34% calc. on the unrecovered fluoroacetate) was filtered off, washed with methanol, acetone, and ether and dried. The product melted at 202—204°.

Ethyl γγ-dichloro-α-fluoro-α-hydroxymethyl-β-oxobutyrate (II; R = $CHCl_2$, R′ = OEt). Piperidine (1 ml.) and formic acid (6 drops) were added to a stirred mixture of ethyl γγ-dichloro-α-fluoroacetoacetate (115 g.) and paraformaldehyde (16 g.). The mixture was heated on a boiling-water bath until a clear solution resulted, then cooled and distilled. The *hydroxymethyl compound* (95 g., 73%) distilled at 120—130°/0·5 mm. and on redistillation at 115—120°/0·2 mm. it had n_D^{24} 1·4655 (Found: C, 33·8; H, 3·7; F, 8·9. $C_7H_9Cl_2FO_4$ requires C, 34·0; H, 3·6; F, 7·7%).

Ethyl αγ-difluoro-α-hydroxymethyl-β-oxobutyrate (II; R = CH_2F, R′ = OEt). Piperidine (1 ml.), formic acid (5 drops), ethyl αγ-difluoroacetoacetate, (35 g.) [5] and paraformaldehyde (5 g.) gave, as above, the *hydroxy-ester* (11 g., 38%), b. p. 95—100°/0·2 mm. (and considerable tar) (Found: C, 43·2; H, 5·4; F, 19·6. $C_7H_{10}F_2O_4$ requires C, 42·9; H, 5·1; F, 19·4%).

Diethyl α-fluoro-α-hydroxymethylmalonate (II; R = R′ = OEt). Piperidine (2 ml.) and formic acid (10 drops) were added to a stirred mixture of ethyl fluoromalonate [4] (70 g.), paraformaldehyde (18 g.), and ethanol (4 ml.). The mixture was heated on a boiling-water bath

[4] Bergmann, Cohen, and Shahak, *J.*, 1959, 3286.
[5] McBee, Pierce, Kilbourne, and Wilson, *J. Amer. Chem. Soc.*, 1953, **75**, 3152.

until it had become clear (4—5 hr.), and then distilled. Some ethyl fluoromalonate (10 g., 14%) was recovered; the *hydroxy-diester* (50 g., 61%) had b. p. 98—100°/0·2 mm. (Found: C, 46·4; H, 6·4; F, 9·2. $C_8H_{13}FO_5$ requires C, 46·2; H, 6·3; F, 9·1%).

α-Fluoro-α-hydroxymethylmalonamide (II; R = R′ = NH_2). (*a*) The foregoing ester (15 g.) was added to cold aqueous 28% ammonia (50 ml.) and kept at 0° for 48 hr. with occasional shaking. When the mass had become homogeneous, the solvent was removed under reduced pressure and the semisolid residue taken up with ethanol. The amide (5 g., 45%) separated in pure form, m. p. 180—182° (Found: C, 32·0; H, 4·8; F, 13·2. Calc. for $C_4H_7FN_2O_3$: C, 32·0; H, 4·7; F, 12·7%).

(*b*) 38% Formaldehyde solution (5 ml.) was added dropwise, with shaking, to a suspension of fluoromalonamide (3 g.) in 28% aqueous ammonia (20 ml.). The resulting clear solution was brought to dryness under reduced pressure and the residue recrystallized from hot aqueous ethanol (yield, 2 g., 58%).

Ethyl α-fluoro-β-methanesulphonyloxypropionate. Crude ethyl γγ-dichloro-α-fluoro-α-hydroxymethyl-β-oxobutyrate [from ethyl γγ-dichloro-α-fluoroacetoacetate (212 g.) and paraformaldehyde (22 g.)] was added dropwise to a stirred solution of sodium carbonate (106 g.) in water (1 l.). Stirring was continued for 1 hr., then the mixture was extracted with ether. Distillation of the ether extract gave the *ester* (III) (30 g., 23%), b. p. 70—72°/0·5 mm., n_D^{25} 1·4251.

Pyridine (17·6 g.) was added dropwise to a mixture of the ester (28 g.), methanesulphonyl chloride (22·5 g.), and benzene (100 ml.), and the mixture was refluxed for 2 hr., diluted with water, and extracted with benzene. The benzene extract was distilled, to yield 20 g. (45%) of the *methanesulphonate*, b. p. 120—125°/0·1 mm., n_D^{25} 1·4467 (Found: C, 33·9; H, 4·9. $C_6H_{11}FO_5S$ requires C, 33·6; H, 5·1%).

Diethyl α-fluoro-α-methanesulphonyloxymethylmalonate. Pyridine (30 g.) was added dropwise and with stirring to a solution of ester (II; R = R′ = OEt) (76 g.) and methanesulphonyl chloride (44 g.) in benzene (100 ml.), and the mixture was refluxed for 2 hr., then cooled and extracted with water. The benzene solution gave, upon fractionation, the *sulphonate* (67 g., 64%), b. p. 140—145°/0·5 mm. (Found: C, 36·6; H, 5·4; F, 7·2. $C_9H_{15}FO_7S$ requires C, 37·8; H, 5·2; F, 6·7%).

Diethyl α-fluoro-α-phthalimidomethylmalonate (V). The foregoing methanesulphonate (40 g.), potassiophthalimide (26 g.), and dimethylformamide (120 ml.) were refluxed, with stirring, for 2 hr., diluted with ether (500 ml.), and extracted with ether (3 × 150 ml.). The combined ether extracts were washed with water, dried (Na_2SO_4), concentrated to about 80 ml., and chilled for 12 hr. The *phthalimido-compound* (19 g., 40%), m. p. 60—80°, was filtered off and could be used in the next step without further purification. For analysis, it was purified by recrystallization from cold methanol, then from toluene–light petroleum and had m. p. 93—94° (Found: C, 58·6; H, 5·1. $C_{16}H_{16}FNO_6$ requires C, 57·0; H, 4·8%).

β-Amino-α-fluoropropionic acid hydrochloride. The ester (V) (23 g.) was refluxed in 36% hydrochloric acid (110 ml.) and water (40 ml.) with stirring for 8 hr., then left overnight at room temperature. The filtered solution was brought to dryness *in vacuo* and the residue taken up again in water (50 ml.), filtered, and brought to dryness again. The solid residue was taken up in methanol, and the insoluble (4 g., 41%) *salt* was filtered off and washed with methanol and anhydrous ether. The yield of the air-dried hydrochloride, m. p. 190—915° (decomp., after sintering at 180°), was 4 g. (41%) (Found: C, 24·8; H, 5·4; Cl, 24·5; F, 13·5; N, 9·5. $C_3H_7ClFNO_2$ requires C, 25·1; H, 4·9; Cl, 24·8; F, 13·3; N, 9·8%).

On Whatman paper (No. 1), with butanol–acetic acid–water (75 : 15 : 10) and phenol, saturated with water, as moving phases, respectively, the following R_F values were found: (I) 0·08 and 0·37; Heidelberger's preparation 0·08 and 0·37; unsubstituted β-alanine 0·23 and 0·57.

INSTITUTE FOR BIOLOGICAL RESEARCH,
NESS-ZIONA, ISRAEL.

[*Received, February 8th*, 1961.]

914. *Heterocyclic Derivatives of Guanidine. Part IV.*[1]

By J. E. Banfield.

Preparation of a number of new guanidino-2*H*-pyrroles required for spectroscopic study is described.

Experimental.—Ultraviolet absorption spectra were determined for 95% EtOH solutions on a Unicam S.P. 500 spectrophotometer by Mrs. J. E. Banfield, B.Sc. General methods, referred to below, correspond to analogous preparations described in Part I.[2] For a description and correlation of spectra referred to below, for convenience, as Type E or Type I, see Part I; [2] " points of inflection " for shoulders are taken as points of maximum upwards curvature [$d^3(\log \varepsilon)/d\lambda^3 = 0$], as points where $d^2(\log \varepsilon)/d\lambda^2 = 0$ (two per shoulder) are widely separated and difficult to locate for curves of this type. Microanalyses were carried out by Dr. K. W. Zimmermann and his staff.

5-N-*Ethylguanidino*-2-*imino*-3,4-*diphenyl*-2H-*pyrrole*. *N*-Ethylguanidinium sulphate (4·5 g.), sodium (0·9 g.), and *trans*-αβ-dicyanostilbene (6 g.) gave, by the previous method, the 2H-*pyrrole* (5·7 g.), m. p. 202° (decomp.) (Found: C, 72·3; H, 6·0; N, 22·0. $C_{19}H_{19}N_5$ requires C, 71·9; H, 6·0; N, 22·1%), which recrystallised from ethanol in yellow prisms (Found: C, 71·6; H, 5·9; N, 22·2%); however, when heating during this recrystallisation was prolonged, the compound separated in brown crystals of lower purity. It had $\lambda_{max.}$ 311, 230, $\lambda_{infl.}$ 374, 214 mμ (log ε 4·262, 4·301, 3·40, 4·28) changed by acetic acid to $\lambda_{max.}$ at 307, $\lambda_{infl.}$ 380 mμ (log ε 4·259, 3·21), both spectra being of Type E.[2]

N′-*Acetylguanidino*-2-*acetylimino*-5-N-*ethyl*-3,4-*diphenyl*-2H-*pyrrole*. 5-*N*-Ethylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (1·0 g.) in acetic anhydride (15 ml.) and stirred at 80—90° until homogeneous yielded the *diacetyl derivative* (from benzene–light petroleum) in orange-yellow needles, m. p. 205·5—209·5° (decomp.) [Found: C, 68·6; H, 5·85; N, 17·15; O, 8·8; Ac, *ca.* 23% (MeOH–NaOH used; the microanalyst reported distillation of a solid). $C_{23}H_{23}N_5O_2$ requires C, 68·8; H, 5·8; N, 17·45; O, 8·0; 2Ac, 21·4%], $\lambda_{max.}$ 344, 235, $\lambda_{infl.}$ 394, 250 mμ (log ε 4·429, 4·416, 3·40, 4·31), and changed by acetic acid to $\lambda_{max.}$ 344, $\lambda_{infl.}$ 384, 250 mμ (log ε 4·341, 3·52, 4·28), both spectra of Type E.

5-N-*Ethylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole*. 5-*N*-Ethylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (2 g.) was treated in ethanolic-aqueous acetic acid with sodium nitrite (4 g.) to yield, after 3 days at 0—5° 5-imino-2-oxo-3,4-diphenyl-3-pyrroline, m. p. 233—236° (0·45 g.), which, purified from ethanol, had m. p. and mixed m. p. 242—245° (decomp.) (Found: C, 77·1; H, 4·8%), and, by basification of the mother liquors, the *oxopyrrole* (1·4 g.), m. p. 214° (decomp.) (Found: N, 17·3%), which (from ethanol) crystallised in bright yellow needles, m. p. 217° (decomp.) (Found: C, 71·65; H, 5·7; N, 17·6; O, 6·1. $C_{19}H_{18}N_4O$ requires C, 71·7; H, 5·7; N, 17·6; O, 5·0%), $\lambda_{max.}$ 316, 230, $\lambda_{infl.}$ 364, 244 mμ (log ε 4·269, 4·228, 3·38, 4·18), changed by alkali to $\lambda_{max.}$ 315, $\lambda_{infl.}$ 364, 237 mμ (log ε 4·275, 3·35, 4·23), both of Type E, and by acetic acid to $\lambda_{max.}$ 351, 277, $\lambda_{infl.}$ 250 mμ (log ε 3·651, 4·140, 4·09), of Type I.

N-*Cyclohexylguanidine*. The sulphate [3] from cyclohexylamine and *S*-methylisothiouronium sulphate afforded a *picrate*, m. p. 230—231° (from ethanol) (Found: C, 42·3; H, 5·1; N, 22·1. $C_{13}H_{18}N_6O_7$ requires C, 42·2; H, 4·9; N, 22·7%).

5-N-*Cyclohexylguanidino*-2-*imino*-3,4-*diphenyl*-2H-*pyrrole*. *N*-Cyclohexylguanidine sulphate (7·5 g.), sodium ethoxide (from sodium, 0·9 g.); and *trans*-αβ-dicyanostilbene (6 g.) afforded (after one week) the 2H-*pyrrole* (7·7 g.), m. p. 215° (decomp.) (Found: C, 74·5; H, 6·9; N, 18·7. $C_{23}H_{25}N_5$ requires C, 74·4; H, 6·8; N, 18·85%), $\lambda_{max.}$ 234, 319, $\lambda_{infl.}$ 367 mμ (log ε 4·331, 4·314, 3·59), changed by acetic acid to $\lambda_{max.}$ 310, $\lambda_{infl.}$ at 384 mμ (log ε 4·260, 3·25), both spectra of Type E, which (from ethanol) formed yellow needles, m. p. 214° (decomp.), of the *monoethanol solvate* (Found: C, 72·3; H, 7·2; N, 17·1. $C_{25}H_{31}N_5O$ requires C, 71·9; H, 7·5; N, 16·8%), $\lambda_{max.}$ 234, 318, $\lambda_{infl.}$ 369 mμ (log ε 4·343, 4·331, 3·59), changed by acetic acid to $\lambda_{max.}$ 310, $\lambda_{infl.}$ 385 mμ (log ε 4·284, 3·26), both spectra of Type E.

[1] Part III, Banfield, *J.*, 1961, 4332.
[2] Banfield, *J.*, 1960, 2108.
[3] McGuinness, unpublished work.

Reaction of the above components for 10 min. on the steam-bath afforded an amorphous yellow-green solid (2·3 g.), which crystallised from ethanol in yellow needles, m. p. 214—216° (decomp.).

The 2*H*-pyrrole and ethyl cyanoacetate afforded 2,5-di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-3-pyrroline (from butan-1-ol), m. p. and mixed m. p. 254—256°.

2-*Acetylimino*-5-N-*cyclohexylguanidino*-3,4-*diphenyl*-2H-*pyrrole*. 5-*N*-Cyclohexylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (1 g.), stirred with acetic anhydride (15 ml.) at 60—70° and then at 0°, yielded the *monoacetyl derivative* (0·95 g.), m. p. 175—178°, which recrystallised from benzene–light petroleum in orange-yellow needles, m. p. 173—176° (decomp.) (Found: C, 71·3; H, 6·3; N, 15·1; O, 7·9. $C_{27}H_{29}N_5O_2$ requires C, 71·2; H, 6·4; N, 15·4;. O, 7·0%), $\lambda_{max.}$ 347, 233, $\lambda_{infl.}$ 390, 250, 217 mμ (log ε 4·474, 4·376, 3·49, 4·29, 4·42), changed by acetic acid to $\lambda_{max.}$ 346, $\lambda_{infl.}$ 390, 250 mμ (log ε 4·393, 3·46, 4·26), both spectra of Type E.

5-N-*Cyclohexylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole*. (*a*) The imino-compound (2·0 g.) and sodium nitrite (4 g.) gave a nitrite salt (2·0 g.), m. p. 142° (decomp.) (Found: N, 15·3%), of unknown constitution. This (0·4 g.) was dissolved in ethanolic acetic acid, and the solution was basified with aqueous sodium carbonate, giving a solid (0·34 g.), m. p. 159—163° (decomp.), which (from methanol) gave the *monomethanol solvate* of 5-N-*cyclohexylguanidino*-2-*imino*-3,4-*diphenyl*-2H-*pyrrole* in yellow needles, m. p. 194° (decomp.) (Found: C, 71·3; H, 7·0; N, 17·4; O, 3·4. $C_{24}H_{29}N_5O$ requires C, 71·4; H, 7·2; N, 17·4; O, 4·0%), $\lambda_{max.}$ 322, 237, $\lambda_{infl.}$ 367 mμ (log ε 4·343, 4·365, 3·59), changed by acetic acid to $\lambda_{max.}$ 309, $\lambda_{infl.}$ 384 mμ (log ε 4·259, 3·27), both spectra of Type E.

Thus the imino-compound has (partly) survived these conditions. The nitrite salt (0·5 g.) was taken up in warm chloroform and diluted with ether, to yield yellow needles of a nitrite salt (0·23 g.), m. p. 154—160° (decomp.) (Found: C, 59·0; H, 6·1; N, 18·8. Calc. for $C_{23}H_{24}N_4O,2HNO_2$: C, 59·0; H, 6·0; N, 17·9. Calc. for $C_{23}H_{25}N_5,HNO_2,2H_2O$: C, 60·8; H, 6·65; N, 18·5%), $\lambda_{max.}$ 311, $\lambda_{infl.}$ 387, 230 mμ (log ε 4·258, 3·224, 4·25), changed by alkali to $\lambda_{max.}$ 322, 234, $\lambda_{infl.}$ 370 mμ (log ε 4·345, 4·420, 3·54), and by acetic acid to $\lambda_{max.}$ 307, $\lambda_{infl.}$ 387 mμ (log ε 3·253, 3·21); all three spectra being of Type E which argues against formulation as the nitrite of the oxo-compound.

(*b*) The imino-compound (1·7 g.) was treated with acidified sodium nitrite (3 g.) at 15—20°; a solid was deposited immediately (probably the nitrite salt of the starting material) which dissolved during 0·5 hr. at *ca.* 40°. The mixture was set aside for 1 week and then refrigerated to yield what is possibly a high-melting *modification* of diphenylmaleinimide, m. p. 222°, thick yellow needles (Found: C, 77·3; H, 4·8; N, 5·9. $C_{16}H_{11}NO_2$ requires C, 77·1; H, 4·45; N, 5·6%). The mother-liquors were basified to give the *oxo-pyrrole* in yellow prisms, m. p. 214—216° (decomp.) (Found: C, 73·8; H, 6·5; N, 15·4%), which crystallised from ethanol in yellow needles, m. p. 213—214° (decomp.) (Found: 73·7; H, 6·5; N, 14·8; O, 5·4. $C_{23}H_{24}N_4O$ requires C, 74·2; H, 6·5; N, 15·0; O, 4·3%), $\lambda_{max.}$ 318, 242, 231, $\lambda_{infl.}$ 374 mμ (log ε 4·338, 4·206, 4·235, 3·32), of Type E, changed by acetic acid to $\lambda_{max.}$ 353, 277, $\lambda_{infl.}$ 247 mμ (log ε 3·712, 4·191, 4·12) of Type I and by alkali to $\lambda_{max.}$ 318, $\lambda_{infl.}$ 227, 240, 365 mμ (log ε 4·353, 4·269, 4·23, 3·49), of Type E.

5-N-*Methylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole*. 2-Imino-5-*N*-methylguanidino-3,4-diphenyl-2*H*-pyrrole [2] (1 g.) and sodium nitrite (2 g.) at 0—5° gave in 6 days a solid (0·5 g.) which afforded 5-imino-2-oxo-3,4-diphenyl-3-pyrroline (0·35 g.), m. p. 246—250° (from ethanol), and, by basification, the *dihydrate* of the *oxo-compound*, m. p. 210° (decomp.) (Found: C, 64·0; H, 6·0; N, 16·6. $C_{18}H_{16}N_4O,2H_2O$ requires C, 64·5; H, 5·9; N, 16·5%), $\lambda_{max.}$ 316, 230, $\lambda_{infl.}$ 364, 237 mμ (log ε 4·291, 4·243, 3·41, 4·22) of Type E, changed by acetic acid to $\lambda_{max.}$ 357, 276; $\lambda_{infl.}$ 250 mμ (log ε 3·712, 4·182, 4·12) of Type I, and by alkali to $\lambda_{max.}$ 315, $\lambda_{infl.}$ at 364, 237 mμ (log ε 4·317, 3·44, 4·28), of Type E. This, when dried at 150°/0·05 mm., gave the anhydrous *oxo-compound*, m. p. 212° (decomp.) (Found: C, 70·5; H, 4·9; N, 18·7; O, 6·2. $C_{18}H_{16}N_4O$ requires C, 71·0; H, 5·3; N, 18·4; O, 5·3%).

2-*Acetylimino*-5-NN-*dimethylguanidino*-3,4-*diphenyl*-2H-*pyrrole*. 5-*NN*-Dimethylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole [2] (1·0 g.) was warmed gently with acetic anhydride (10 ml.) and the solution was cooled in ice, giving the yellow *monoacetyl derivative* (0·75 g.) (from benzene–light petroleum), m. p. 218—219° (decomp.) (Found: C, 70·3; H, 6·1; N, 19·25; O, 5·1; Ac, 13·9, but with unsatisfactory saponification. $C_{21}H_{21}N_5O$ requires C, 70·2; H, 5·9; N, 19·5; O, 4·5; Ac, 12·0%), $\lambda_{max.}$ 237, 338, $\lambda_{infl.}$ 384 mμ (log ε 4·402, 4·390, 3·62) of Type E, changed by acetic acid to $\lambda_{max.}$ 297, $\lambda_{infl.}$ 334 mμ (log ε 4·285, 3·98), of Type intermediate between E and I.

5-NN-*Dimethylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole*. The imino-compound (2·0 g.) and sodium nitrite (4·0 g.), when mixed and acidified at 0—5° and refrigerated for 4 days, afforded the *nitrite* (1·25 g.), m. p. 200—208° (decomp.) (Found: C, 62·75; H, 5·54; N, 19·05; O, 12·8. $C_{19}H_{19}N_5O_3$ requires C, 62·45; H, 5·2; N, 19·2; O, 13·1%), $\lambda_{max.}$ 309, $\lambda_{infl.}$ 362 mμ (log ε 4·193, 3·71), changed by alkali to $\lambda_{max.}$ 311, $\lambda_{infl.}$ 370 mμ (log ε 4·298, 3·50), both spectra of Type E and by acid to $\lambda_{max.}$ 279, $\lambda_{infl.}$ 332 mμ (log ε 4·174, 3·81), essentially of Type I; although the acid concentration was apparently less than that used below. The filtrate was basified to yield a yellow solid (0·8 g.) which (from ethanol) afforded (probably) the oxo-compound, m. p. 251° decomp.) (Found: C, 71·2; H, 5·8%), $\lambda_{max.}$ 230, 317, $\lambda_{infl.}$ 380 mμ (log ε 4·266, 4·267, 3·33), changed by acetic acid to $\lambda_{max.}$ 282, 354 mμ (log ε 4·134, 3·707).

This (0·2 g.) was taken up in ethanolic acetic acid and added to aqueous sodium carbonate solution, giving a solid, m. p. 249—250° (decomp.) (0·2 g.), which, dissolved in acetic acid and treated with ethanolic triethylamine, gave the *oxo-compound* in yellow needles, m. p. 252—253° (decomp.) (Found: C, 71·7; H, 5·8; N, 18·0; O, 5·1. $C_{19}H_{18}N_4O$ requires C, 71·7; H, 5·7; N, 17·6; O, 5·0%), $\lambda_{max.}$ 314, 234, $\lambda_{infl.}$ 374 mμ (log *D* 0·279, 0·788, 1·40), of Type E, changed by acetic acid to $\lambda_{max.}$ 278, 353, 234, 374 mμ (log *D* 0·296, 0·367, 1·440), of Type E in a nearly saturated solution, the base being almost insoluble in ethanol.

2-*Methylthio*-2-*imidazoline sulphate*. A mixture of 2-thioimidazoline (72 g.), dimethyl sulphate (35 ml.), and water (20 ml.) was refluxed for 3 hr., then diluted with water; a solid, m. p. 198—200°, and probably unchanged thioimidazoline, was collected and the filtrate was evaporated; the residue was taken up in a little water and stirred into acetone, giving the sulphate (64 g.) in hygroscopic crystals which, although slightly wet, were suitable for the succeeding preparation. A further amount of the sulphate (13 g.) was obtained from the mother-liquors. The sulphate afforded a picrate, m. p. 183—186° (lit.,[4] 180°).

2-*Amino*-2-*imidazoline sulphate*. The above-mentioned sulphate (20 g.) and aqueous ammonia (*d* 0·880; 40 ml.) were mixed and refluxed for 1·5 hr., the solvent was removed, and the residual oil was dissolved in a minimum of water and added to acetone. The precipitated oil slowly crystallised and the solid recrystallised from methanol–acetone to give the sulphate (11 g., not thoroughly dried), m. p. 248° (lit.,[4] 281°). The picrate, as first prepared, had m. p. 217—221° (lit.,[4] 217, 219°); however, when purified from water it had m. p. 220—220·5° (Found: C, 34·5; H, 3·2; N, 26·35. Calc. for $C_9H_{10}N_6O_7$: C, 34·4; H, 3·2; N, 26·75%); recrystallisation of the impure picrate from ethanol gave a solid of m. p. 259—261° (decomp.).

2-(5-*Imino*-3,4-*diphenyl*-5H-2-*pyrrolylimino*)*imidazolidine*. 2-Amino-2-imidazoline sulphate (5·5 g.), sodium (0·9 g.), and *trans*-αβ-dicyanostilbene (5·5 g.) were caused to react, initially at 50° and subsequently at room temperature, yellow crystals of an *ethanol solvate*, m. p. 172° (decomp.), separating (Found: C, 71·6; H, 6·0%). This recrystallised from ethanol in yellow needles, decomp. *ca.* 208°, but not molten below 250° (Found: C, 72·15; H, 5·6; N, 18·8; O, 1·5%). Another sample, dried at 100°/0·05 mm., decomposed similarly at *ca.* 210° (Found: C, 71·1; H, 5·85; N, 21·3; O, 1·3. $C_{19}H_{17}N_5,\frac{1}{2}C_2H_6O$ requires C, 71·1; H, 5·9; N, 20·6; O, 2·4%), $\lambda_{max.}$ 321, 234, $\lambda_{infl.}$ 367 mμ (log ε 4·324, 4·324, 3·49), changed by acetic acid to $\lambda_{max.}$ 321, $\lambda_{infl.}$ 387 mμ (log ε 4·257, 3·25), both spectra of Type E.[2] This sample lost *ca.* 10% by weight at 140—160°/0·05 mm. to give the *base* (Found: C, 72·4; H, 5·5; N, 21·85. $C_{19}H_{17}N_5$ requires C, 72·4; H, 5·4; N, 22·2%).

The iminopyrrole, heated with ethyl cyanoacetate, gave 2,5-di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-3-pyrroline (m. p. and mixed m. p.).

The iminopyrrole (0·5 g.) was taken up in ethanolic acetic acid, diluted with water, and basified with sodium carbonate, giving a yellow solid (0·42 g.), which afforded unchanged iminopyrrole as yellow needles, darken at 207°, not melted by 273°. However, treatment of the ethanolic acetic acid solution with sodium nitrite gave at 3° (after 5 min.) a 27% yield of 5-imino-2-oxo-3,4-diphenyl-3-pyrroline, m. p. 248—252° (decomp.) (Found: C, 76·7; H, 5·0; N, 11·0%), and longer reaction times gave both this and diphenylmaleinimide; none of the expected 2-(5-oxo-3,4-diphenyl-5*H*-2-pyrrolylimino)imidazoline being obtained.

The iminopyrrole (1·0 g.) was covered with acetic anhydride (5 ml.), set aside at room temperature and then refrigerated; it gave colourless rhombs of *diacetyl derivative* (0·39 g.), m. p. 188—190° (from benzene) (Found: C, 68·5; H, 5·3; N, 17·7; O, 8·7; Ac, 21·6. $C_{23}H_{21}N_5O_3$ requires 69·15; H, 5·3; N, 17·5; O, 8·0; 2Ac, 21·6%), $\lambda_{max.}$ 262, 215 mμ (log ε

[4] Beilstein's "Handbuch der Organischen Chemie," Springer Verlag, Berlin.

3·817, 4·450), changed but slightly by acetic acid to $\lambda_{max.}$ 262 mμ (log ε 3·820). The structure of this derivative is being further investigated.

The author thanks the Research Committee of the University of New England for a grant.

UNIVERSITY OF NEW ENGLAND,
N.S.W., AUSTRALIA.

[*Received, March 6th*, 1961.]

---

915. *The Characterisation of Amines by Use of (−)-Di-O-p-toluoyltartaric Acid.*

By D. A. A. KIDD.

(−)-DI-*O*-*p*-TOLUOYLTARTARIC ACID, first prepared by Stoll and Hofmann [1] for the resolution of racemic lysergic hydrazide, was later used in the separation of the ergotoxine group of alkaloids,[2] for characterisation of minor alkaloids of the *Rauwolfia* genus,[3] and for resolution of an intermediate in the synthesis of reserpine.[4] Incidentally to its use for *Rauwolfia* alkaloids,[5] this acid, now commercially available, has been found invaluable in the characterisation and purification of a variety of synthetic amines, many of which give hygroscopic or non-crystalline salts with most acids. We have prepared its salts with

				Found (%)		Required (%)	
Base	M. p.	Recryst. from	Formula	C	H	C	H
n-Propylamine	186—188°	Aq.MeOH	$C_{26}H_{26}N_2O_8$	61·9	7·1	61·9	7·2 [b]
Isopropylamine	202—204 [a]	Aq.MeOH	$C_{23}H_{27}NO_8$	62·0	6·05	62·0	6·1
n-Butylamine	191—192	MeOH	$C_{24}H_{29}NO_8$	62·8	6·4	62·7	6·4
s-Butylamine	201—202 [a]	MeOH	$C_{24}H_{29}NO_8$	62·8	6·6	62·7	6·4
Dimethylamine	186—188	EtOH	$C_{22}H_{25}NO_8$	60·95	5·75	61·2	5·8
Di-n-propylamine	170—171	EtOH	$C_{26}H_{33}NO_8$	64·25	6·9	64·1	6·8
Di-n-butylamine	174—175	Aq.EtOH	$C_{28}H_{37}NO_8$	64·9	7·2	65·2	7·2
Dicyclohexylamine	186—187 [a]	EtOH	$C_{32}H_{41}NO_8$	67·75	7·25	67·7	7·3
Triethylamine	157—157·5 [a]	EtOH	$C_{26}H_{33}NO_8$	64·2	6·85	64·1	6·8
Benzylamine	195—197	MeOH	$C_{27}H_{27}NO_8$	65·6	5·7	65·7	5·5
Dibenzylamine	150—150·5	Aq.EtOH	$C_{34}H_{33}NO_8$	70·1	5·8	70·0	5·7
Aniline	159—161	EtOAc	$C_{26}H_{25}NO_8$	65·3	5·2	65·2	5·3
o-Toluidine	167—169	EtOAc	$C_{27}H_{27}NO_8$	65·5	5·8 [c]	65·7	5·5
m-Toluidine	164—164·5	C_6H_6–EtOAc	$C_{27}H_{27}NO_8$	66·2	5·55 [d]	65·7	5·5
p-Toluidine	167—168	C_6H_6–EtOAc	$C_{27}H_{27}NO_8$	65·6	5·5 [e]	65·7	5·5
p-Chloroaniline	171·5—173·5	Pet [f]–EtOAc	$C_{26}H_{24}ClNO_8$	60·9	4·6	60·8	4·7
α-Naphthylamine	168—170	Pet [f]–EtOAc	$C_{30}H_{27}NO_8$	68·2	5·25	68·0	5·1
β-Naphthylamine	186—187	EtOH	$C_{30}H_{27}NO_8$	68·3	5·3	68·0	5·1
Pyridine	143—145 [a]	Aq.EtOH	$C_{25}H_{23}NO_8$	64·5	5·0	64·5	5·0
α-Picoline	157—158 [a]	EtOH	$C_{26}H_{25}NO_8$	65·7	5·3	65·2	5·3
β-Picoline	174—175 [a]	EtOH–EtOAc	$C_{26}H_{25}NO_8$	65·4	5·65	65·2	5·3
γ-Picoline	140—141·5 [a]	EtOH	$C_{26}H_{25}NO_8$	64·9	5·1	65·2	5·3
2-Ethylpyridine	147·5—148·5 [a]	EtOH	$C_{27}H_{27}NO_8$	66·1	5·7	65·7	5·5
4-Ethylpyridine	150—151 [a]	EtOH	$C_{27}H_{27}NO_8$	65·5	5·4	65·7	5·5
4-Benzylpyridine	123·5—125 [a]	EtOH	$C_{32}H_{29}NO_8$	69·3	5·5	69·2	5·3
Piperidine	172—173 [a]	EtOH	$C_{25}H_{29}NO_8$	63·5	6·25	63·7	6·2
Pyrrolidine	184—186 [a]	EtOH	$C_{24}H_{27}NO_8$	63·1	6·1	63·0	5·95
Morpholine	183—184·5 [a]	EtOH	$C_{24}H_{27}NO_9$	60·8	5·7	60·9	5·75

[a] With decomp. [b] Found: N, 5·6. Required: N, 5·55%. [c] Found: N, 2·8. Required: N, 2·8%. [d] Found: N, 2·9. Required: N, 2·8%. [e] Found: N, 3·05. Required: N, 2·8%. [f] Pet. is light petroleum (b. p. 60—80°).

a number of common amines (see Table). Salt formation, which normally results in an acid (1 : 1) salt although a few neutral (2 : 1) salts were obtained, can be carried out in organic solvents or by double decomposition in water, but use of ether solutions has the

[1] Stoll and Hofmann, *Helv. Chim. Acta*, 1943, **26**, 922.
[2] Stoll and Hofmann, *Helv. Chim. Acta*, 1943, **26**, 1570.
[3] Hofmann, *Helv. Chim. Acta*, 1954, **37**, 314; Stoll, Hofmann, and Brunner, *ibid.*, 1955, **38**, 270.
[4] Woodward, Bader, Bickel, Frey, and Kierstead, *Tetrahedron*, 1958, **2**, 50.
[5] Kidd, *J.*, 1958, 2432.

advantage that all the salts are insoluble whereas the acid, and usually the amine, are soluble. The salts are normally stable and crystalline, have definite melting points, and recrystallise from the usual solvents without decomposition. The substantial increase in molecular weight is useful in characterising small quantities of amine, which can be regenerated, for example, by shaking a solution of the salt in chloroform–methanol with aqueous alkali. For identification the fact that the melting points appear to fall within a range of about 60° is a disadvantage, although useful separations occur in certain groups of related amines, such as the picolines.

Experimental.—(−)-*Di*-O-p-*toluoyltartaric anhydride.* Stoll and Hofmann's method [1] was modified by the use of a solvent: A mixture of (+)-tartaric acid (164 g.), *p*-toluoyl chloride (575 g.), and xylene (825 ml.) was stirred under reflux with exclusion of moisture. After 3 hr., the clear hot solution was poured into cold benzene (2 l.). The anhydride, after being washed with hot benzene, and recrystallised if necessary from ethyl acetate, melted at 204—205°.

(−)-*Di*-O-p-*toluoyltartaric acid.* Prepared essentially by Stoll and Hofmann's method,[1] the acid had m. p. 169—171°, $[\alpha]_D^{22}$ −141° (*c* 1·0 in EtOH), but some samples showed pronounced earlier softening, or even complete melting, at ~150° without change in optical rotation or microanalysis. The dextrorotatory form behaves similarly [6] in exhibiting a double m. p. (148°, 172°).

Salts. The *salts* (see Table) were prepared by mixing ethereal solutions of equimolecular quantities of acid and base. Analyses indicated 1 : 1 salts except in the one case noted. Several other salts have been described elsewhere.[7]

The author thanks Mr. B. W. Sharp for technical assistance.

THE RESEARCH LABORATORIES,
MAY & BAKER LTD., DAGENHAM, ESSEX. [*Received, April 26th,* 1961.]

[6] Hunt, *J.*, 1957, 1926.
[7] Collins, *J.*, 1960, 2053.

---

916. *Steroids of Unnatural Configuration. Part VI.* Oxidation and Reduction of Epilumisterol.*

By G. D. MEAKINS and M. W. PEMBERTON.

PREVIOUS work in this series established that oxidation [1] and reduction [2] of the 5,6-double bond in lumisterol (I) generally lead to products formed by attack at the front (β) face of the molecule. Since inversion of the 3-hydroxyl group in lumisterol from the β- to the α-configuration should accentuate this difference from normal steroid behaviour we have investigated the corresponding reactions of epilumisterol (lumista-5,7,22-trien-3α-ol) (II; R = H).[3]

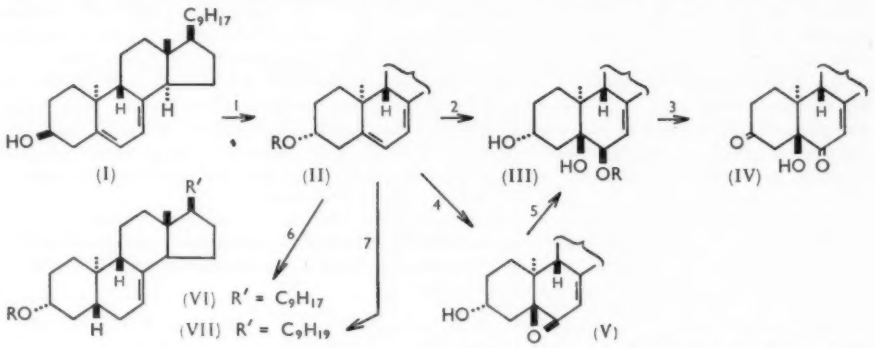
The lumisterol–epilumisterol complex, obtained from lumisterol with aluminium isopropoxide in boiling xylene, was separated with digitonin,[3] to give epilumisterol which was purified through its 3,5-dinitrobenzoate.. Although ring A of lumisterol and epilumisterol is somewhat distorted from the chair form by the ring B diene system the substituents at position 3 retain characteristic conformations (3β-axial,3α-equatorial).

With osmium tetroxide epilumisterol gave a triol shown to be the 3α,5β,6β-compound (III; R = H) by oxidation with chromic acid to the 5β-hydroxy-3,6-dione (IV).[1] The 5β,6β-epoxide (V) was the first product formed from epilumisterol and 1 mol. of perbenzoic acid: a longer reaction time in the presence of added benzoic acid led to an

* Part V, *J.*, 1960, 2800.

[1] Mayor and Meakins, *J.*, 1960, 2792.
[2] Castells, Fletcher, Jones, Meakins, and Swindells, *J.*, 1960, 2785.
[3] Barnett, Heilbron, Jones, and Verrill, *J.*, 1940, 1390.

intermediate, presumably the triol monobenzoate (III; R = Bz), which was reduced with lithium aluminium hydride to triol (III; R = H). Reduction of epilumisterol with lithium and ethanol in liquid ammonia afforded the 5β-dihydro-compound [2] (VI; R = H) while catalytic reduction produced the 5β-tetrahydro-compound [2] (VII; R = H), both



Reagents: 1, $Al(OPr^i)_3$. 2, OsO_4. 3, CrO_3 in $COMe_2$. 4, BzO_2H–C_6H_6. 5, BzO_2H–BzOH–C_6H_6. 6, Li–NH_3–EtOH. 7, H_2–Pt in AcOH.

reactions giving high yields. These results correspond closely with those established for lumisterol, except that catalytic reduction of lumisterol yielded approximately equal proportions of products containing the 5α- and the 5β-configuration.

Experimental.—For general directions see *J.*, 1958, 2156.

Lumista-5,7,22-trien-3α-ol (*epilumisterol*) (II; R = H). The lumisterol–epilumisterol complex [3] (5 g.; m. p. 157—159°, $[\alpha]_D$ +195°) in ethanol (450 ml.) and water (50 ml.) was added to digitonin (8·5 g.) in ethanol (765 ml.) and water (85 ml.) at 60°. The digitonide of epilumisterol, which separated as the mixture cooled, was collected and the dried material (9 g.) heated in pyridine (150 ml.) at 90° for 90 min. Evaporation at 100°/15 mm. followed by two extractions (Soxhlet) of the residue with dry ether gave epilumisterol (2·2 g.; soluble in ether) which was purified as the 3,5-dinitrobenzoate (2·8 g.), m. p. 185—186° (from ethyl acetate–ethanol), $[\alpha]_D$ +131° (*c* 1·1) {lit.,[4] m. p. 184—185°, $[\alpha]_D$ +134° (in benzene)}. Hydrolysis on alkaline alumina afforded epilumisterol (1·7 g.), m. p. 112—113° (from acetone–methanol), $[\alpha]_D$ +221° (*c* 1·0), $\nu_{max.}$ 3540 and 1052 cm.$^{-1}$ (lit.,[4] m. p. 112—113°, $[\alpha]_D$ +227°). The acetate (II; R = Ac) had m. p. 115—116° (from ethanol), $[\alpha]_D$ +129° (*c* 0·8), $\nu_{max.}$ 1730 and 1242 (simple acetate band) cm.$^{-1}$ (lit.,[5] m. p. 114—115°, $[\alpha]_D$ +175°).

Oxidation of lumista-5,7,22-trien-3α-ol. (*a*) A solution of epilumisterol (500 mg.) and osmium tetroxide (500 mg.) in dry ether (40 ml.) and pyridine (2 ml.) was kept at 20° for 3 days, and then refluxed with lithium aluminium hydride (400 mg.) for 2 hr. Standard treatment gave *lumista-7,22-diene-3α,5β,6β-triol* (III; R = H) (350 mg.), m. p. 228—231° (from aqueous methanol), $[\alpha]_D$ −21° (*c* 0·6) (Found: C, 78·3; H, 11·0. $C_{28}H_{46}O_3$ requires C, 78·1; H, 10·8%). Oxidation of the triol (100 mg.) in acetone with 8N-chromic acid gave 5β-hydroxylumista-7,22-diene-3,6-dione (IV) (50 mg.), m. p. 182—184°, $[\alpha]_D$ −20° (*c* 0·8), identified by comparison with authentic material.[1]

(*b*) Epilumisterol (210 mg.) in benzene (15 ml.) and xylene (1·5 ml.) was oxidised with 0·068M-perbenzoic acid in benzene (7·9 ml.) for 20 hr. at 5° and the solution was then poured on a column of deactivated alumina (25 g.). Elution with benzene–ether (9 : 1) gave 5β,6β-*epoxylumista-7,22-dien-3α-ol* (V) (100 mg.), m. p. 160—161° (from acetone), $[\alpha]_D$ +76° (*c* 1·1) (Found: C, 81·65; H, 10·9. $C_{28}H_{44}O_2$ requires C, 81·5; H, 10·75%), $\nu_{max.}$ 3590 and 1047 cm.$^{-1}$.

Benzoic acid (85 mg.) was added to a solution containing epilumisterol and perbenzoic acid in the quantities specified above. The mixture was kept at 5° for 4 days and then chromatographed. Ether eluted material [assumed from spectroscopic examination to be the triol

[4] Harrison, Hurst, Lythgoe, and Williams, *J.*, 1960, 5176.
[5] Heilbron, Kennedy, Spring, and Swain, *J.*, 1938, 869.

monobenzoate (III; R = Bz)] which was reduced with lithium aluminium hydride to the 3α,5β,6β-triol (III; R = H) (35 mg.), m. p. and mixed m. p. 226—229°, $[\alpha]_D$ −20° (*c* 0·6).

Reduction of lumista-5,7,22-trien-3α-ol. (*a*) Lithium (200 mg.) was added to a stirred solution of epilumisterol (250 mg.) in dry ether (20 ml.) and liquid ammonia (40 ml.), and after 30 min. ethanol (~4 ml.) was added slowly. Chromatography of the product on deactivated alumina (20 g.) gave 5β-lumista-7,22-dien-3α-ol (VI; R = H) [200 mg.; eluted with benzene–ether (4 : 1; 50 ml.)], m. p. 137—139° (from ethanol), $[\alpha]_D$ +47° (*c* 0·8), identified by comparison with authentic material [2] and preparation of the 3,5-dinitrobenzoate,[2] m. p. 166—168°.

(*b*) A solution of epilumisterol (775 mg.) in glacial acetic acid was shaken in hydrogen with Adams catalyst (95 mg.). The product, isolated after the absorption of *ca.* 2·1 mol. of hydrogen, was treated with lithium aluminium hydride (to remove acetylated material) and then chromatographed, giving 5β-lumist-7-en-3α-ol (VII; R = H) (500 mg.), m. p. 144—145° (from ethanol), $[\alpha]_D$ +60° (*c* 0·7), identified by comparison with authentic material [2] and preparation of the acetate (VII; R = Ac), m. p. 115—119°, $[\alpha]_D$ +5° (*c* 0·5).[2]

The authors are indebted to Professor E. R. H. Jones, F.R.S., for his interest and advice, to the Department of Scientific and Industrial Research for a maintenance grant (to M. W. P.), and to Mrs. I. E. Croxon for technical assistance.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, April 27th,* 1961.]

---

917. *The First Acid Dissociation Constant of Hydrogen Sulphide at High Pressures.*

By A. J. ELLIS and D. W. ANDERSON.

PREVIOUS papers [1-3] showed the large effect of pressure on the ionisation of weak acids of the hydrated gas type such as " carbonic acid " and " sulphurous acid," compared with simple weak acids such as acetic and phosphoric acid. The work on carbon dioxide was part of a programme on the chemistry of mineral deposition under high pressures and high temperatures. Results are now given from conductance measurements at 25° of the effect of pressure on the ionisation of hydrogen sulphide, also a dissolved gas weak acid and important in natural mineral-forming processes.

Experimental.—Materials and apparatus. Hydrogen sulphide was prepared by the reaction of " AnalaR " sodium sulphide with dilute sulphuric acid. Pure nitrogen was passed for an hour through the distilled water (specific conductance $1{\cdot}4 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$) used for making the sulphide solutions. Potassium hydrogen sulphide solutions were prepared by titrating hydrogen sulphide solutions to pH 9·3 with potassium hydroxide.

The apparatus used was similar to that described previously.[1]

Method. Previous values [1] for the conductance of potassium chloride and hydrochloric acid were combined with the present results for hydrogen sulphide and potassium hydrogen sulphide to provide values of K_a for hydrogen sulphide.

Corrections for the conductance of the distilled water were made as before.[1]

At the concentrations of hydrogen sulphide used (0·01—0·001m), ionization is less than 1%. Within this degree of accuracy the concentrations of un-ionized hydrogen sulphide can be equated to the total sulphide in solution. The first molal dissociation constant, K_a, was obtained from the equation

$$K_a = m^{-1}\gamma_\pm^2\,(1000L'/\Lambda'\rho_r)^2,$$

i.e.,

$$L' = 10^{-3}\Lambda'\rho_r K_a^{\frac{1}{2}}\, m^{\frac{1}{2}}/\gamma_\pm.$$

The symbols are as defined in the previous papers.

At the low ion concentrations (~10^{-5}m) the value for the sum of the molar conductances

[1] Ellis, *J.*, 1959, 3689.
[2] Clark and Ellis, *J.*, 1960, 247.
[3] Ellis and Anderson, *J.*, 1961, 1765.

Λ' of the H^+ and HS^- ions can be taken as constant at each pressure, and the value of $\gamma_\pm$ equated to unity.

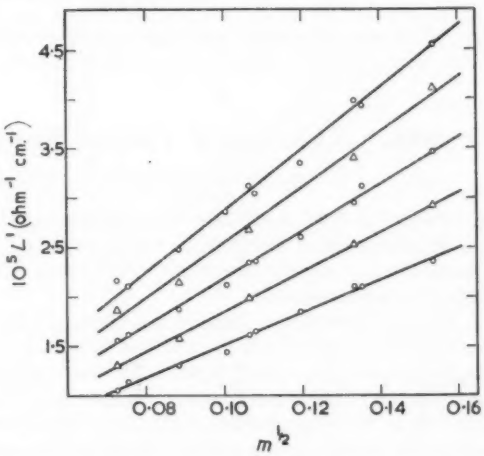
By plotting L' against $m^{\frac{1}{2}}$, a line of slope $10^{-3}\Lambda'\rho_r K_a^{\frac{1}{2}}$ was obtained for each pressure, and hence the value of K_a obtained.

Bright platinum electrodes were used in the conductance cell as it was considered this would minimize their interaction with the sulphide solutions. To check any polarisation effects, results were obtained for several different oscillator frequencies. Table 1 gives typical values of L' (ohm^{-1} $cm.^{-1}$) for a solution of hydrogen sulphide.

TABLE 1.

Hydrogen sulphide: variation in L' with oscillator frequency (values of 10^{-5} L').

Frequency (cycles/sec.)	P (atm.)			Frequency (cycles/sec.)	P (atm.)		
	1	1000	2000		1	1000	2000
500	2·07	2·86	3·80	2000	2·16	3·01	4·06
1000	2·10	2·95	3·99	5000	2·18	3·05	4·12



Specific conductance (L' in ohm^{-1} $cm.^{-1}$) for hydrogen sulphide as a function of $m^{\frac{1}{2}}$.

Curves relate, reading downwards, to 2000, 1500, 1000, 500, and 1 atm.

The ratios of high- and low-pressure L' values are constant above 1000 cycles and this frequency was used throughout, for convenience. Similar small frequency effects were observed with bright gold electrodes.

Results.—Table 2 gives for potassium hydrogen sulphide the values of $\Lambda^P\rho_r/\Lambda^1$, which within experimental error were constant at concentrations below 10^{-2}m. Table 3 contains the values of $\Lambda'\rho_r$ used for calculating K_a.

The Figure presents the specific conductance of hydrogen sulphide solutions as a function of $m^{\frac{1}{2}}$ at the different pressures. Table 4 contains the values of K_a derived from the results shown in the Figure, and the change in partial molar volume on ionization at one atmosphere (ΔV^1).

TABLE 2.

Potassium hydrogen sulphide: values of $\Lambda^P\rho_r/\Lambda^1$ at 25° for 10^{-3}m-solutions.

(Value of Λ^1 in parentheses.)

P (atm.)	1	500	1000	1500	2000
$\Lambda^P\rho_r/\Lambda^1$	(139)	1·030	1·045	1·055	1·065

TABLE 3.

Values of $\Lambda^1\rho_r$ used in calculation of K_a.

P (atm.)	1	500	1000	1500	2000
$\Lambda'\rho_r$	417	439	454	467	480

TABLE 4.

First acid dissociation constant, K_a, for hydrogen sulphide at 25°.

P (atm.)	1	500	1000	1500	2000
$10^7 K_a$	1·54	2·10	2·76	3·56	4·25

$\Delta V^1 = -15{\cdot}0$ c.c. mole^{-1}.

Discussion.—The effect of pressure on the first dissociation constant of hydrogen sulphide is less than that for the dissolved gases carbon dioxide [1] ($\Delta V^1 = -26{\cdot}5$), sulphur dioxide [3] ($\Delta V^1 = -19{\cdot}7$), and ammonia [4] ($\Delta V^1 = -28{\cdot}9$). ΔV^1 for hydrogen sulphide is similar to that for other simple weak acids, for which the values range from about −7 to −16 c.c. mole^{-1} (*e.g.*, salicylic,[2] formic,[4] benzoic,[2] acetic,[3] and phosphoric acid:[3] −7·2, −8·8, −10·6, −12·1, and −15·5 c.c. mole^{-1}, respectively). It is therefore confirmed that large negative ΔV^1 values arise only where hydration equilibria are involved in the ionization processes, for example, with carbon dioxide, sulphur dioxide, and ammonia.

DOMINION LABORATORY, DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH,
WELLINGTON, NEW ZEALAND. [*Received, May 8th*, 1961.]

[4] Hamann, "Physico-chemical Effects of Pressure," Butterworths, London, 1957.

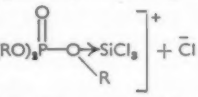
---

918. *Interaction of Trialkyl Phosphates with Silicon Chlorides.*

By M. J. FRAZER, W. GERRARD, and A. P. SINGH.

RELEVANT to studies of the factors influencing the formation of mixed anhydride links in the development of inorganic or semi-inorganic polymers [1] is the observation that triethyl phosphate and silicon tetrachloride gave ethyl chloride and silicon phosphate,[2] and we now give additional examples.

Silicon tetrachloride (3 mol.) and the trialkyl (Pr^i, Bu^i, Bu^s) phosphate (4 mol.) reacted very slowly at 20° (Table 1), and had to be heated for effective evolution of alkyl chloride and formation of Si–O–P links. The methyl ester reacted vigorously at 20°, and with the n-propyl and n-butyl esters reaction was well advanced in 24 hr. The removal of alkyl from the phosphorus–oxygen bond would appear to be by an S_N2 reaction (end-on approach) involving the chlorine anion, which could be formed by attachment of oxygen to silicon as shown. Attachment by the phosphoryl-oxygen appears less likely; because, although trialkyl phosphates [3] and triphenyl phosphate [4] readily form complexes with boron trichloride at that oxygen atom, triphenyl phosphate did not react with silicon tetrachloride, in accordance with low electron density on the aryloxy-oxygen atom owing to mesomeric interaction of that atom with the phenyl group.



Tri-n-butyl phosphite and silicon tetrachloride react by the mutual exchange of alkoxyl and chlorine,[5] phosphorus and silicon remaining separate in chloro-esters. Similarly, the n-butoxysilanes and boron trichloride react by the mutual exchange of alkoxyl and chlorine, although for the s-butyl compounds formation of Si–O–B links is evident.[6]

In conformity, there was no significant interaction between ethyl phosphorodichloridate and silicon tetrachloride under the conditions stated, electron density on the oxygen atoms

[1] Gerrard, "Reports of Progress in Applied Chemistry," 1960, *J. Oil Colour Chemists' Assoc.*, 1959, **42**, 625.
[2] Gerrard and Jeacocke, *Chem. and Ind.*, 1959, 704.
[3] Gerrard and Griffey, *J.*, 1960, 3170.
[4] Frazer, Gerrard, and Patel, *J.*, 1960, 726.
[5] Gerrard and Honey, unpublished work.
[6] Frazer, Gerrard, and Strickson, *J.*, 1960, 4701.

being effectively reduced by the two chlorine atoms attached to phosphorus. On the other hand, tri-n-butoxychlorosilane (*n* mol.) afforded a silyl phosphate, probably $[(Bu^nO)_3SiO]_nP(O)(OR)_{3-n}$, and alkyl chloride (Table 2), when heated with a trialkyl phosphate (1 mol.) (for Me or Et, instead of Bu^n when $n = 1$, see ref. 7). Some tetra-alkoxysilane was found; this could arise from the monochlorosilane by mutual exchange of groups, and the polymeric non-volatile residue is accounted for by interaction of the resulting dichlorosilane and the phosphate.

Experimental.—Trialkyl phosphate–silicon tetrachloride systems. The trialkyl phosphate (4 mol.) was added to silicon tetrachloride (3 mol.) at 20°. Trimethyl phosphate reacted vigorously at 20°: methyl chloride and silicon tetrachloride were evolved and were condensed at −80°. The mixture became a gel within 2 hr. Gel formation occurred overnight in experiments 2 and 4 (Table 1). The progress of the reaction at 20° was followed by determining the easily hydrolysable chlorine (e.h.Cl) in samples (0·2 g.). After 195 hr., at 20°, alkyl chloride, unchanged phosphate, and silicon tetrachloride were removed at the stated temperature and pressure. Volatile products were separated by distillation and characterised by their physical constants, analysis, and gas chromatography. Propene (4·20 g.) and butene (3·80 g.) were detected in experiments 2 and 4, and in all the experiments (except no. 1), hydrogen chloride (0·5—1·5 g.) was evolved during the heating. After the removal of the volatile matter, part of the residual black solid was heated at 900° in air, a white powder corresponding to $Si_3P_4O_{16}$ being formed.

TABLE 1.

Experiment no.	1	2	3	4	5	6
R in $(RO)_3PO$	Me	Pr^n	Pr^i	Bu^n	Bu^i	Bu^s
e.h.Cl (%) in mixtures at 20°: 2 hr.	—	—	—	25·5	—	—
e.h.Cl (%) in mixtures at 20°: 24 hr.	0	11·3	30·4	12·3	27·1	25·9
e.h.Cl (%) in mixtures at 20°: 48 hr.	—	8·7	30·4	11·6	27·1	24·6
e.h.Cl (%) in mixtures at 20°: 195 hr.	—	8·4	30·4	11·0	26·9	20·7
Calc. e.h.Cl (%) for orig. mixture	39·8	30·3	30·3	27·1	27·1	27·1
RCl was removed at:	20° [a]	20°/15 mm.	85°/10 mm. (5 hr.)	20°/13 mm.	130° (8 hr.)	150°/10 mm. (5 hr.)
Total RCl (mol.)	4·4 [b]	9·29	8·01	8·91	8·94	9·90
Unchanged $SiCl_4$ (mol.)	1·75 [b]	0·29	0·52	0·33	0·60	0·29
Solid [d] obtained at 900° (P, %)	28·2	27·1	26·6	27·9	27·3	25·4
(Si, %)	17·1	19·4	17·2	17·5	17·6	18·2

[a] Unchanged phosphate (1·30 mol.) obtained at 130°/15 mm. [b] Evolved during the initial exothermal reaction. [c] Bu^tCl 95%, and Bu^tCl 5%. [d] Calc. for $O_{16}P_4Si_3$: P, 26·7; Si, 18·1%.

TABLE 2.

R in $(RO)_3PO$ (*n* mol.)	Et	Bu^n	Et	Bu^n
$(Bu^nO)_3SiCl$ (*n* mol.), *n* =	1	1	2	3
RCl (mol.)	0·86	0·97	2·0	2·75
Silyl phosphate, yield (%)	69·8 [a]	56·5 [b]	20·1 [b]	25·0 [b]
B. p. at 0·1 mm.	148—150°	168—172°	160—166°	170—185°
$[R]_D$, Found: [c]	100 (99)	117 (117)	163 (156)	220 (213)
P (%), Found: [c]	7·9 (7·7)	6·6 (6·8)	3·7 (5·0)	2·1 (3·7)
Si (%), Found: [c]	7·1 (7·0)	5·9 (6·1)	8·2 (9·0)	8·7 (10·0)
M, Found: [c]	398 (400)	462 (456)	—	—

[a] Also $(Bu^nO)_4Si$ (24·0%), b. p. 110°/12 mm. (Found: Si, 8·5%). [b] Other fractions were obtained. Physical constants and analysis showed these to be mixtures of the tetra-alkoxysilane and the silyl phosphate, but they could not be separated by ordinary distillation. [c] Calc. values for $[(Bu^nO)_3SiO]_nPO(OR)_{3-n}$ are in parentheses.

Triphenyl phosphate–silicon tetrachloride. A mixture of triphenyl phosphate (58·60 g., 1 mol.) and silicon tetrachloride (1 mol.) was heated under reflux at 160° for 20 hr. Silicon tetrachloride was recovered at 20°/18 mm., and triphenyl phosphate (99·8%), m. p. 48° (Found: P, 9·0. Calc. for $C_{18}H_{15}O_4P$: P, 9·5%), remained.

[7] Feher, Kühlborsch, Blümcke, Keller, and Lippert, *Chem. Ber.*, 1957, **90**, 134.

Ethyl phosphorodichloridate and silicon tetrachloride. Ethyl phosphorodichloridate (51·40 g., 1 mol.) and silicon tetrachloride (1 mol.) were heated under reflux at 90° for 35 hr. Ethyl chloride (1·50 g.) (gas chromatography), silicon tetrachloride (97·3% recovery), b. p. 56° (Found: Cl, 82·9%), and the phosphorodichloridate (45·80 g., 89·1% recovery), b. p. 62°/10 mm., n_D^{20} 1·4336 (Found: Cl, 43·1. Calc. for $C_2H_5Cl_2O_2P$: Cl, 43·5%), were obtained.

Trialkyl phosphates and tri-n-butoxychlorosilane. Tri-n-butoxychlorosilane (1, 2, and 3 mol.) and the phosphate (1 mol., see Table 2) were heated under reflux at 150—155° for 6 hr. Alkyl chloride, and then fractions containing the tetra-alkoxysilane, and the alkyl butoxysilyl phosphates, and a residue containing silicon and phosphorus were obtained.

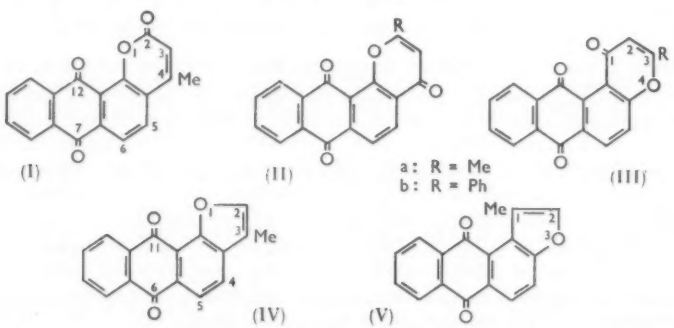
THE NORTHERN POLYTECHNIC, HOLLOWAY ROAD,
LONDON, N.7.

[*Received, May 11th,* 1961.]

919. *Hydroxyanthracene Series. Part IV.*[1] *Synthesis of Some Anthraquinone Derivatives.*

By N. H. SHAH and SURESH SETHNA.

THE quinonopyrones (I—III) have been prepared by oxidising the corresponding anthrapyrones with chromic acid or sodium dichromate in acetic acid; yields were good. Kostanecki–Robinson benzoylation of 2-acetyl-1-hydroxy- and 1-acetyl-2-hydroxy-anthraquinone yielded the 2- and the 3-benzoyl derivative of compounds (IIIb and IIb, respectively); Kostanecki–Robinson acetylation gave resins.



Attempts to synthesise ketones by Fries migration of 1- and 2-acetoxyanthraquinone or Friedel–Crafts acetylation of 1- and 2-hydroxyanthraquinone did not succeed. These ketones were, however, obtained in good yield by oxidation of 2-acetyl-1-acetoxy- and 1-acetyl-2-acetoxy-anthracene with chromic acid in acetic acid and subsequent hydrolysis with sulphuric acid.

3-Methylanthra[1,2-*b*]furan[1] on oxidation gave 2-acetyl-1-hydroxyanthraquinone instead of the quinono-furan (IV). The desired furan derivatives (IV and V) were, however, synthesised by oxidising the intermediate compounds, ethyl 2-acetyl-1- and ethyl 1-acetyl-2-anthryloxyacetate[1,2] to the corresponding anthraquinone derivatives, hydrolysis of the esters to the corresponding acids, and simultaneous cyclisation and decarboxylation by hot sodium acetate and acetic anhydride.

Experimental.—Oxidations (see Table). To a stirred solution of the anthracene derivative (0·01 mole) in acetic acid at 60—65° was added, during 10 min., a 10% solution of chromic acid or sodium dichromate (0·04 mole) in 90% acetic acid. After 3 hours' stirring at this temperature the mixture was left overnight at room temperature. The *products* obtained on dilution were washed with cold dilute alkali and the residue crystallised from acetic acid.

[1] Part III, Shah and Sethna, *J. Indian Chem. Soc.*, 1960, **37**, 699.
[2] Shah and Sethna, *J. Org. Chem.*, 1959, **24**, 1783.

Products formed by chromic oxidation.

Product [a]	M. p.	Yield (%)	Found (%) C	Found (%) H	Formula	Reqd. (%) C	Reqd. (%) H
Anthraquinones							
1-Acetoxy-2-acetyl [b]	167—168°	35	70·4	3·6	$C_{18}H_{12}O_5$	70·1	3·9
2-Acetoxy-1-acetyl [b]	200—202	45	70·2	4·1	,,	,,	,,
1-Acetyl-2-methoxy [c]	215—216	45	73·2	4·1	$C_{17}H_{12}O_4$	72·9	4·3
Et x-*acetyl*-9,10-*dihydro*-9,10-*dioxo*-y-*anthryloxyacetates*							
$x = 2, y = 1$	145—146	46	68·0	4·6	$C_{20}H_{16}O_6$	68·2	4·6
$x = 1, y = 2$	164—165	46	68·4	4·8	,,	,,	,,
7,12-Dihydro-4-methyl-2,7,12-trioxo-2*H*-anthra[1,2-*b*]pyran (I)	319—320	54	74·3	3·1	$C_{18}H_{10}O_4$	74·5	3·5
7,12-*Dihydro*-4,7,12-*trioxo*-4H-*anthra*[1,2-*b*]*pyrans* (II)							
2-Methyl	293 [d]	36	74·7	4·0	,,	,,	,,
2-Phenyl	325	37	78·8	3·7	$C_{23}H_{12}O_4$	78·4	3·4
7,12-*Dihydro*-1,7,12-*trioxo*-1H-*anthra*[2,1-*b*]*pyrans* (III)							
2-Methyl	251	27	74·2	3·4	$C_{18}H_{10}O_4$	74·5	3·5
2-Phenyl	266—267	27	78·0	3·8	$C_{23}H_{12}O_4$	78·4	3·4

[a] Insol. in alkali; give a red colour with Zn dust and alkali. [b] As the reaction caused partial hydrolysis the crude product was treated with acetic anhydride and pyridine for 24 hr. at room temperature. [c] Also obtained by methylation of 1-acetyl-2-hydroxyanthraquinone. [d] With decomp.

1-*Acetoxy*-2-*acetylanthracene*, prepared from 2-acetyl-1-anthrol,[3] acetic anhydride, and pyridine overnight at room temperature, crystallised from dilute alcohol in yellow needles, m. p. 140—142° (Found: C, 77·7; H, 4·9: $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%).

2-*Acetoxy*-1-*acetylanthracene*, prepared as above from 1-acetyl-2-anthrol,[3] crystallised from dilute alcohol in colourless needles, m. p. 130° (Found: C, 77·5; H, 4·5%).

2-*Acetyl*-1-*hydroxyanthraquinone*. 1-Acetoxy-2-acetylanthraquinone (0·1 g.) was hydrolysed by concentrated sulphuric acid (5 ml.) at room temperature in 4 hr. The product crystallised from dilute acetic acid in reddish-yellow needles, m. p. 166° (Spruit [4] gave the same m. p.) (Found: C, 72·1; H, 3·9. Calc. for $C_{16}H_{10}O_4$: C, 72·2; H, 3·8%). It gave a green colour with alcoholic ferric chloride. Its 2,4-*dinitrophenylhydrazone* crystallised from acetic acid in reddish needles, m. p. 276° (Found: N, 12·7. $C_{22}H_{14}N_4O_7$ requires N, 12·6%).

3-*Benzoyl*-7,12-*dihydro*-4,7,12-*trioxo*-2-*phenyl*-4H-*anthra*[1,2-*b*]*pyran*. A mixture of 2-acetyl-1-hydroxyanthraquinone (0·6 g.), fused sodium benzoate (1·8 g.), and benzoic anhydride (6 g.) was heated at 180—190° for 8 hr. The *product* obtained on removal of the excess of benzoic anhydride and sodium benzoate with hot water crystallised from acetic acid in yellow needles (0·15 g.), m. p. 275—276°. (Found: C, 78·5; H, 3·9. $C_{30}H_{16}O_5$ requires C, 78·9; H, 3·5%).

This compound (0·1 g.) with boiling 70% w/v sulphuric acid (10 ml.) (2 hr.) gave the debenzoylated product that crystallised from acetic acid as yellow needles, m. p. and mixed m. p. 325° (cf. Table).

1-*Acetyl*-2-*hydroxyanthraquinone*. 1-Acetyl-2-acetoxyanthraquinone (0·25 g.) was hydrolysed with sulphuric acid as above. The *product* crystallised from dilute acetic acid in brown needles, m. p. 249—250°, giving a pale green colour with alcoholic ferric chloride (Found: C, 72·0; H, 3·6%). Its 2,4-*dinitrophenylhydrazone* crystallised from alcohol in red needles, m. p. 260° (Found: N, 12·8%).

2-*Benzoyl*-7,12-*dihydro*-1,7,12-*trioxo*-3-*phenyl*-1H-*anthra*[2,1-*b*]*pyran*. 1-Acetyl-2-hydroxyanthraquinone (0·8 g.), sodium benzoate (2·4 g.), and benzoic anhydride (8 g.) gave as above the *quinono-pyran* as yellow needles (0·1 g.), m. p. 253—254° (from acetic acid) (Found: C, 78·7; H, 3·5%).

The same product was obtained on oxidation of 2-benzoyl-1-oxo-3-phenylanthra[2,1-*b*]-pyran [2] (0·1 g.) in acetic acid with sodium dichromate at room temperature.

2-*Acetyl*-9,10-*dihydro*-9,10-*dioxo*-1-*anthryloxyacetic acid*. Ethyl 2-acetyl-1-(9,10-dihydro-9,10-dioxoanthryloxy)acetate (0·25 g.) was hydrolysed by 4% sodium hydroxide solution (25 ml.) at 50° for about an hour. The *acid* obtained on acidification crystallised from dilute

[3] Lele, Shah, and Sethna, *J. Org. Chem.*, 1956, **21**, 1293.
[4] Spruit, *Rec. Trav. chim.*, 1949, **68**, 304.

acetic acid in yellow needles (0·2 g.), m. p. 189—190° (Found: C, 66·2; H, 3·9. $C_{16}H_{12}O_6$ requires C, 66·7; H, 3·7%).

6,11-*Dihydro*-3-*methyl*-6,11-*dioxoanthra*[1,2-*b*]*furan*. The above acid (0·2 g.) and anhydrous sodium acetate (1 g.) were boiled in acetic anhydride (10 ml.) for 45 min. The *product* was washed with alkali and crystallised from dilute acetic acid in reddish-yellow needles, m. p. 226—227° (Found: C, 77·9; H, 3·7. $C_{17}H_{10}O_3$ requires C, 77·9; H, 3·8%).

1-*Acetyl*-9,10-*dihydro*-9,10-*dioxo*-2-*anthryloxyacetic acid*. Ethyl 1-acetyl-2-(9,10-dihydro-9,10-dioxoanthryloxy)acetate (0·15 g.) on hydrolysis as above gave the corresponding acid, yellowish-green plates (0·1 g.) (from dilute alcohol), m. p. 256—257° (decomp.) (Found: C, 66·4; H, 3·8%).

6,11-*Dihydro*-1-*methyl*-6,11-*dioxoanthra*[2,1-*b*]*furan*. The preceding acid (0·2 g.), acetic anhydride (10 ml.) and anhydrous sodium acetate (1 g.) were boiled for 45 min. The *product* was washed with cold dilute alkali and crystallised from alcohol in pale yellow plates, m. p. 198—199° (Found: C, 77·4; H, 3·9%).

CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE, M.S. UNIVERSITY OF BARODA, BARODA, INDIA. [*Received, May 16th*, 1961.]

---

920. *Constituents of* Eugenia maire *A. Cunn. Part II.*[1] *Identification of Mairin and Constituents of the Leaves.*

By LINDSAY H. BRIGGS and R. C. CAMBIE.

IN Part I[1] there was reported the isolation of 3,3′,4-tri-*O*-methylellagic acid and an alleged dihydroxytriterpene, mairin, from the bark of *Eugenia maire*. Continued investigation of mairin has now shown its identity with betulic acid.

The leaves of *E. maire* also afforded betulic acid, and, in minor amount, oleanolic acid; gallic acid, methyl gallate, and β-sitosterol were also isolated but not 3,3′,4-tri-*O*-methylellagic acid or leucoanthocyanins. Oleanolic acid has been isolated by other workers from *E. caryophyllata* Thunbg.[2]

Experimental.—Analyses were by Dr. A. D. Campbell and his associates, University of Otago, New Zealand. Infrared spectra were measured for KBr discs with a Beckman IR2 instrument; optical rotations were measured for $CHCl_3$ solutions.

Betulic acid. "Mairin," m. p. 295—296°, in benzene solution, was chromatographed on silica gel. Fractions eluted from the column with benzene and crystallised from methanol gave betulic acid, m. p. and mixed m. p. 312—314°, $[\alpha]_D^{25}$ +10·8° (*c* 1·2) (correct infrared spectrum). The acetate had m. p. and mixed m. p. 291—292° [Found (for sample dried to constant wt.): C, 77·35; H, 9·7; Ac, 8·0. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1; Ac, 8·6%]. The benzoate had m. p. and mixed m. p. 339—341° [Found (for sample dried to constant wt.): C, 79·0; H, 9·35. Calc. for $C_{37}H_{52}O_4$: C, 79·2; H, 9·35%].

Further working-up of the initial extract of the bark of *E. maire* and chromatography on silica gel of the fraction soluble in benzene gave additional betulic acid (7·14 g. from 7·1 kg.).

Leaves. Dried, finely ground leaves (1 kg.) were extracted (Soxhlet) with methanol and the residue, after removal of solvent, was re-extracted with hot ether. The ether concentrate was treated with 20% aqueous sodium hydroxide (3 × 200 c.c.) and acidic material isolated through the insoluble sodium salts by Corbett and McDowall's procedure.[3] Repeated crystallisation from methanol gave betulic acid (6·4 g.), m. p. and mixed m. p. 310—312°, $[\alpha]_D^{25}$ +10·6° (*c* 0·89) (correct infrared spectrum). The acetate had m. p. and mixed m. p. 290—292° [Found (for sample dried to constant wt.): C, 77·3; H, 10·0; Ac, 8·9%]; the methyl ester had m. p. and mixed m. p. 225—226°.

Oleanolic acid. Acidification of the aqueous alkaline solution above gave amorphous acids which were washed with hot water and chromatographed in benzene on silica gel. Elution

[1] Part I, Briggs, Cambie, Lowry, and Seelye, *J.*, 1961, 642.
[2] Karrer, "Konstitution und Vorkommen der Organischen Pflanzenstoffe," Birkhäuser Verlag, Basle, 1958, p. 806.
[3] Corbett and McDowall, *J.*, 1958, 3715.

with benzene gave, first, further betulic acid (1·8 g.), then oleanolic acid (38 mg.), $[\alpha]_D^{25}$ +71·3° (*c* 0·87), m. p. and mixed m. p. 297—299° (correct infrared spectrum). The methyl ester had m. p. and mixed m. p. 198—200°.

Gallic acid. The aqueous washings and the acidified aqueous solution remaining after separation of amorphous acids were continuously extracted with ether for 30 hr. The concentrated ether solution was extracted with 10% aqueous sodium hydrogen carbonate, and the extract was acidified and re-extracted with ether. Removal of solvent and repeated crystallisation from water gave gallic acid (1·1 g.), m. p. and mixed m. p. 256—258° (decomp.) after drying at 125° (Found: C, 49·5; H, 3·7. Calc. for $C_7H_6O_5$: C, 49·4; H, 3·6%).

Methyl gallate. Purification of the neutral fraction obtained from the ether solution above by Jurd's method,[4] followed by repeated crystallisation from water, gave methyl gallate (65 mg.), m. p. and mixed m. p. 197—198° (decomp.) (Found: C, 52·2; H, 4·2. Calc. for $C_8H_8O_5$: C, 52·2; H, 4·4%).

β-*Sitosterol.* Chromatography of the neutral fraction of the initial ether extract in light petroleum on alumina (P. Spence and Co., grade H) and crystallisation from methanol of fractions eluted from the column with benzene gave β-sitosterol (125 mg.), m. p. and mixed m. p. 137—138°, $[\alpha]_D^{25}$ −34·6° (*c* 0·61) [Found (for sample dried to constant wt.): C, 84·2; H, 12·3. Calc. for $C_{29}H_{50}O$: C, 84·0; H, 12·15%] (correct infrared spectrum). The acetate had m. p. and mixed m. p. 126—127° (Found: C, 81·6; H, 11·35. Calc. for $C_{31}H_{52}O_2$: C, 81·5; H, 11·5%).

We are indebted to Dr. R. E. Corbett, University of Otago, for samples of betulic acid and methyl oleanolate and to Professor D. E. White, University of Western Australia, for a sample of oleanolic acid. Assistance is gratefully acknowledged from the Chemical Society, the Rockefeller Foundation of New York, the Australian and New Zealand Association for the Advancement of Science, and the Research Grants Committee of the University of New Zealand.

Department of Chemistry,
University of Auckland, New Zealand. [*Received, May 24th,* 1961.]

[4] Jurd, *J. Amer. Chem. Soc.*, 1956, **78**, 3445.

---

921. *The Direct Amination of Mesitylene by Hydrazoic Acid in Concentrated Sulphuric Acid.*

By G. M. Hoop and J. M. Tedder.

The recent papers by Kovacic and Bennett on "Direct Amination" [1] prompt us to report some uncompleted work carried out in these laboratories two years ago and since set aside. Schmidt was the first to report the direct amination of benzene by sodium azide in concentrated sulphuric acid.[2] He suggested that the NH-radical was involved. It seemed to us more likely that in very strong acids hydrazoic acid would become protonated to yield the -onium ion ($NH=\overset{+}{N}=NH$ or $N\equiv\overset{+}{N}-NH_2$) and that this ion was responsible for the amination. Cryoscopic examination in 99·8% sulphuric acid showed that sodium azide gives an *i* factor of ~4: $NaN_3 + 2H_2SO_4 \longrightarrow H_2N_3^+ + HSO_4^- + Na^+ + HSO_4^-$.

Solutions of sodium azide in concentrated sulphuric acid were found to aminate a wide variety of aromatic nuclei, but the yields of amine were very small. Mesitylene proved exceptional and three amino-compounds, mesidine, diaminomesitylene, and 3-amino-2,4,6-trimethylbenzenesulphonic acid, were isolated together with some polymeric material which had the properties of an aromatic amine. When a solution of sodium azide in concentrated sulphuric acid at 60° was used the main product was the amino-sulphonic acid (42%), and the basic material was mainly diaminomesitylene and polymer. In 90% sulphuric acid under the same conditions no sulphonic acid was formed and the basic product was mainly mesidine. *m*-Xylene yielded only traces of sulphonated amine when treated with sodium azide in concentrated sulphuric acid, and with 87% sulphuric acid the

[1] Kovacic and Bennett, *J. Amer. Chem. Soc.*, 1961, **83**, 221, 743.
[2] Schmidt, *Ber.*, 1924, **57**, 704.

yield of crude *m*-xylidene was only 2%. Other aromatic hydrocarbons gave similar yields. It seems possible that the exceptional behaviour of mesitylene is due to the formation of mesitylenesulphonic acid which is hydrolysed to yield mesitylene dispersed in acid solution. Treatment of mesitylenesulphonic acid with a similar solution of sodium azide in 90% sulphuric acid gave an even larger yield of basic material (corresponding to about 80% of the starting acid), but toluene-*p*-sulphonic acid, which is less easily hydrolysed, yielded only 3-amino-4-methylbenzenesulphonic acid (5%).

The only other aromatic compound which gave more than a few percent of an amino-compound was *p*-nitrotoluene. When treated with a slight excess of sodium azide in concentrated sulphuric acid at 100° for 2 hr. it afforded a moderate yield of a crystalline amine. This product proved to be similar in properties and derivatives to the product that Bamberger isolated on reaction of *p*-tolyl azide with *p*-nitrotoluene and sulphuric acid,[3] and Gattermann obtained on electrolytic reduction of *p*-nitrotoluene.[4] These workers described their product as 4-amino-2′-methyl-5′-nitrodiphenylmethane, and the analysis of the present product and its derivatives are consistent with this structure, although it is not easy to explain its formation.

In an attempt to achieve amination in a more homogeneous medium, benzene and several other aromatic compounds were treated with a solution of toluene-*p*-sulphonyl azide and only a slight excess of sulphuric acid. This mixture gave slightly better yields of aminated product with benzene but more than one compound was produced. With other aromatic compounds the yields were no better than with sodium azide.

The present results show that, except with mesitylene, solutions of hydrazoic acid in sulphuric acid have little value as aminating agents. The results are consistent with a mechanism involving electrophilic substitution, although the exact nature of the acting species remains obscure. The reaction cannot involve hydroxylamine because sodium azide in anhydrous hydrogen fluoride was found to be weakly effective. It seems possible that the -onium ion ($N\equiv\overset{+}{N}-NH_2$) reacts with an aromatic nucleus to yield nitrogen and NH_2^+ as the transient electrophile which partakes in the substitution.[1,5]

Experimental.—Some hydrazoic acid is evolved when sodium azide is dissolved in concentrated sulphuric acid and the solution heated. In all the experiments described the reaction was carried out in an open vessel behind the safety screen of a fume cupboard with a good draught. So long as the vessel is open there is no danger, but in one experiment in a closed vessel fitted with a condenser there was a very violent explosion.

Amination of mesitylene. (*a*) In concentrated sulphuric acid. Sodium azide (8·1 g.) was dissolved in concentrated sulphuric acid (100 c.c.) and the solution was heated at 60°. Mesitylene (6 g.) was added dropwise during 20 min. to the rapidly stirred mixture (heat was evolved during the addition and the temperature was maintained without external heating). Further sodium azide (8·1 g.) was then added slowly and mixture was stirred for a further hour at 60—70°. The acid solution was poured on ice; the precipitate (4·47 g.) formed recrystallised from hot water to yield white crystals of **3-*amino*-2,4,6-*trimethylbenzenesulphonic acid*** which charred at about 400° without melting. It was soluble in alkali and treatment with nitrous acid yielded a diazonium salt (Found: C, 50·2; H, 6·5; N, 6·5; S, 15·7%; equiv., 213. $C_9H_{13}NO_3S$ requires C, 50·2; H, 6·1; N, 6·5; S, 14·9%; equiv., 215). The main aqueous filtrate was rendered alkaline and extracted with ether. Evaporation gave an oil (3·36 g.; N, 12·4%) which on diazotisation and coupling gave a mixture of dyes. Distillation gave no clear fractions but one fraction (0·40 g.; b. p. 130—180°/16 mm.) gave an oil (N, 17·7%) from which **1,3-*dibenzamido*-2,4,6-*trimethylbenzene***, m. p. 278°, was obtained (Found: C, 76·2; H, 6·1; N, 7·4. $C_{23}H_{22}N_2O_2$ requires C, 77·0; H, 6·1; N, 7·8%). In another experiment crystalline 1,2-diamino-2,4,6-trimethylbenzene, m. p. 89°, was obtained. A higher-boiling fraction (1·82 g.; b. p. 180—200°; N, 9·2%) became a glass on cooling but still exhibited the properties of an aromatic amine and could be diazotised and coupled.

[3] Bamberger, *Annalen*, 1925, **443**, 194.
[4] Gattermann, *Ber.*, 1893, **26**, 1844.
[5] Keller and Smith, *J. Amer. Chem. Soc.*, 1944, **66**, 1122; 1946, **68**, 899.

(*b*) In 90% sulphuric acid. Sodium azide (8·1 g.) was dissolved in a mixture of concentrated sulphuric acid (187 g.) and water (14 g.). Mesitylene (6 g.) was added gradually and the whole was heated to 100°. The mesitylene was followed by further sodium azide (8·1 g.), and the mixture was heated at 100° for 2 hr. The products were isolated as before. No precipitate was formed when the reaction mass was poured on ice. The basic product (4·06 g.) was distilled at atmospheric pressure; the main fraction boiled at 230° and was readily converted into a crystalline acetyl derivative, m. p. 213° (mesidine [6] has b. p. 230° and *N*-acetylmesidine has m. p. 210—212°).

Amination of m-*xylene*. (*a*) In concentrated sulphuric acid. *m*-Xylene (5·3 g.) was added to a solution of sodium azide in concentrated sulphuric acid in the conditions used for mesitylene. There was no basic product although there was a small amount of an amino-sulphonic acid as indicated by addition of sodium nitrite to the aqueous mother liquor and coupling of the resultant diazonium salt with β-naphthol.

(*b*) In 87% sulphuric acid. *m*-Xylene (5·3 g.) was added to a solution of sodium azide (8·1 g.) in a mixture of concentrated sulphuric acid (130 g.) and water (14·8 g.). Then further sodium azide (8·1 g.) was added and the mixture heated at 100° for 2 hr. and worked up as before. The aqueous phase contained traces of an amino-sulphonic acid. A crude basic oil (0·13 g.) was also obtained. This was diazotised and coupled with β-naphthol and the resultant dye purified by chromatography to yield 1-(2,4-dimethylphenylazo)-2-naphthol,[7] m. p. 155°, alone or in admixture with an authentic specimen.

Amination of p-*nitrotoluene*. *p*-Nitrotoluene (12·1 g.) was added to a solution of sodium azide (7·8 g.) in concentrated sulphuric acid (50 c.c.). The mixture was heated for 2·5 hr., then poured on ice. Unchanged *p*-nitrotoluene (5·83 g.) was precipitated. The filtrate was rendered alkaline and extracted with ether continuously for 12 hr. Evaporation left dark-yellow crystals (1·28 g.). Two recrystallisations from aqueous alcohol gave yellow needles, m. p. 117° (Found: C, 69·3; H, 6·2; N, 11·7. Calc. for $C_{14}H_{14}N_2O_2$: C, 69·4; H, 5·8; N, 11·6%). Bamberger [3] reports 4-amino-2′-methyl-5′-nitrodiphenylmethane to melt at 117—118°. A portion of the product was treated with acetic anhydride: the resultant *N*-acetyl derivative had m. p. 174° (Gattermann [4] reports m. p. 174°). The product was diazotised and coupled with β-naphthol, to yield 1-[p-(2-*methyl*-5-*nitrobenzyl*)*phenylazo*]-2-*naphthol*, m. p. 157—158° (Found: C, 71·8; H, 5·3; N, 11·1. $C_{24}H_{19}N_3O_3$ requires C, 72·5; H, 4·8; N, 10·7%).

Amination of mesitylenesulphonic acid. Mesitylenesulphonic acid dihydrate (5·9 g.) was added gradually to a solution of sodium azide (4·1 g.) in 90% sulphuric acid (100 g.). Further sodium azide (4·1 g.) was added and the mixture stirred at 100° for 2 hr., then poured on ice and rendered alkaline. Extraction with ether and evaporation left a basic oil (2·85 g.). Distillation at atmospheric pressure gave no discrete fractions but one fraction (b. p. <230°, 0·15 g.) corresponded to mesidine and treatment with acetic anhydride gave 2,4,6-trimethylacetanilide (m. p. 210—212°). A second fraction (b. p. 230—260°; 0·9 g.) was mainly diaminomesitylene, from which the benzoyl derivative, m. p. and mixed m. p. 278°, was obtained.

The authors thank Dr. D. Jaques for measuring the *i*-factor.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, May 26th*, 1961.]

[6] Ingold and Piggott, *J.*, 1924, **125**, 168.
[7] Niementowski, *Anz. Akad. Wiss. Krakau*, 1902, 413 (*Chem. Zentr.*, 1902, II, 938).

922. *Some Compounds Derived from* o-2-*Carboxyethylbenzoic Acid.*

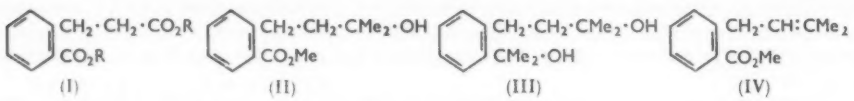
By E. D. ANDREWS and W. E. HARVEY.

o-2-CARBOXYETHYLBENZOIC ACID (I; R = H) is readily available from β-naphthol [1] and we have investigated it with a view to its use in the synthesis of certain *ortho*-substituted isopentylbenzenes.

Nitration of the acid (I; R = H) proceeds normally to give the 5-nitro-compound which was converted into the corresponding amine and bromo-compound. With methylmagnesium iodide the dimethyl ester (I; R = Me) was converted, in good yield, into the

[1] Page and Tarbell, *Org. Synth.*, 1954, **34**, 8.

hydroxy-ester (II), although with a large excess of the Grignard reagent some of the diol (III), isolated as the crystalline hemihydrate, was also formed. Dehydration of the ester (II) with sulphuric acid gave the unsaturated ester (IV), identified by hydrogenation



(I) (II) (III) (IV)

and hydrolysis to *o*-isopentylbenzoic acid, which is more conveniently prepared by this method than by that previously described.[2]

Experimental.—o-2-*Carboxyethylbenzoic acid*. This acid[1] with methanolic hydrogen chloride gave its *dimethyl ester*, b. p. 124°/2·5 mm., n_D^{25} 1·5115 (Found: C, 65·05; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%).

2-2′-*Carboxyethyl*-5-*nitrobenzoic acid*. A mixture of fuming nitric acid (3·25 g., 1 mol.) and concentrated sulphuric acid (6 g.) was added dropwise with stirring to an ice-cold solution of *o*-2-carboxyethylbenzoic acid (15 g.) in concentrated sulphuric acid (50 g.). Stirring was continued for a further 2 hr., then the solution was poured on ice. The *nitro-acid* (16·25 g., 88%) crystallised from water as pale yellow plates, m. p. 180—182° (Found: C, 50·6; H, 3·7; N, 5·7. $C_{10}H_9NO_6$ requires C, 50·2; H, 3·8; N, 5·9%). Treatment with methanol containing 5% of dry hydrogen chloride on the water-bath for 3 hr. and working up in the usual manner gave *methyl* 2-2′-*methoxycarbonylethyl*-5-*nitrobenzoate* (60%), pale yellow needles (from methanol), m. p. 51—52° (Found: C, 54·3; H, 4·6; N, 5·0. $C_{12}H_{13}NO_6$ requires C, 53·9; H, 4·9; N, 5·2%), and 2-2′*methoxycarbonylethyl*-5-*nitrobenzoic acid* (30%), colourless prisms (from methanol), m. p. 124—125° (Found: C, 51·6; H, 4·1; N, 5·5. $C_{11}H_{11}NO_6$ requires C, 52·1; H, 4·4; N, 5·5%).

5-*Amino*-2-2′-*carboxyethylbenzoic acid*. The nitro-acid, in methanol, was hydrogenated at 50°/50 atm. in presence of Raney nickel. The *amino-acid* (86%) crystallised from water as plates, m. p. 200—201° (Found: C, 58·1; H, 5·2; N, 6·3. $C_{10}H_{11}NO_4$ requires C, 57·4; H, 5·3; N, 6·7%). The *dimethyl ester* prepared analogously in 95% yield crystallised from methanol as plates, m. p. 75—76° (Found: C, 60·9; H, 6·1; N, 5·95. $C_{12}H_{15}NO_4$ requires C, 60·75; H, 6·4; N, 5·9%).

5-*Bromo*-2-2′-*carboxyethylbenzoic acid*. Potassium nitrite (5 g.) in water (15 ml.) was added dropwise to a cooled suspension of the amino-acid (10 g.) in 40% hydrobromic acid (50 g.) and water (5 ml.) in a flask which was stoppered after each addition of the nitrite solution and shaken until all the nitrous fumes were absorbed. The temperature was kept below 10°; when most of the nitrite solution had been added a yellow precipitate was formed. Copper bronze (2 g.) was added, and, after the initial reaction, the mixture was allowed to warm to room temperature, then heated on a steam bath for 1 hr. during which the bromo-compound was precipitated. The mixture was treated with 10% sodium carbonate solution and the resulting dark red solution was filtered and acidified with hydrochloric acid. The brown material which separated (8 g., 62%) was sublimed in a high vacuum at 150° to give the colourless *bromo-acid*, m. p. 160—162° (Found: C, 44·3; H, 3·3; Br, 28·8. $C_{10}H_9BrO_4$ requires C, 44·0; H, 3·7; Br, 29·3%).

Reaction of methyl 2-2′-*methoxycarbonylethylbenzoate with methylmagnesium iodide*. The di-ester (48 g., 1 mol.) in dry ether (250 ml.) was added dropwise with stirring during 1 hr. to methylmagnesium iodide (2·5 mol.) in ether (250 ml.). The resulting suspension was heated under reflux with stirring for 1·5 hr., then poured on ice and ammonium chloride. The ethereal solution was washed with water, dried (Na_2SO_4), and concentrated, to yield *methyl* o-(3-*hydroxy*-3-*methylbutyl*)*benzoate* (II) (41 g., 85%), b. p. 115°/1 mm., n_D^{25} 1·5181 (Found: C, 70·05; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·2%). When the amount of methylmagnesium iodide was increased to 5·5 mol. and heating was extended to 3 hr., working up as before gave the above material together with 15% of crystalline material which separated from the crude product and recrystallised from moist light petroleum (b. p. 45—60°) as needles of 4-[o-(1-*hydroxy*-1-*methylethyl*)*phenyl*]-2-*methylbutan*-2-*ol hemihydrate*, m. p. 78—79° [Found (air-dried material): C, 72·5; H, 10·0. $C_{14}H_{22}O_2,\frac{1}{2}H_2O$ requires C, 72·7; H, 10·0%]. When this material was dried in a high vacuum over phosphorus pentoxide at room temperature it formed a viscous

[2] Harvey, *J.*, 1958, 2060.

gum from which the crystalline material was regenerated by crystallisation from moist light petroleum.

o-(3-*Hydroxy*-3-*methylbutyl*)*benzoic acid*. Alkaline hydrolysis of the ester (II) gave the *acid* which crystallised from light petroleum as plates, m. p. 81—82° (Found: C, 69·3; H, 7·7. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%).

o-(3-*Methylbut*-2-*enyl*)*benzoic acid*. The above hydroxy-acid was heated under reflux with vigorous stirring with 40% w/v sulphuric acid for 3·5 hr. The product was isolated with ether and distilled, giving the *acid*, b. p. 140—143°/1 mm., which solidified and after sublimation in a vacuum had m. p. 83—83·5° (Found: C, 76·0; H, 7·6. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

Methyl o-(3-*methylbut*-2-*enyl*)*benzoate* (IV). Dehydration of the ester (II) with sulphuric acid as above gave, in 70% yield, the unsaturated *ester*, b. p. 100—102°/1 mm., n_D^{25} 1·5220 (Found: C, 76·5; H, 8·2. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·9%).

o-*Isopentylbenzoic acid*. The unsaturated ester above, in methanol, was hydrogenated at 50°/50 atm. in presence of Raney nickel, to give methyl *o*-isopentylbenzoate, b. p. 92—93°/1 mm., n_D^{25} 1·4997, identified by alkaline hydrolysis to *o*-isopentylbenzoic acid, m. p. and mixed m. p. 42—43°.

The authors thank Dr. A. D. Campbell, University of Otago, for the microanalyses.

VICTORIA UNIVERSITY OF WELLINGTON,
WELLINGTON, NEW ZEALAND. [*Received, May 29th*, 1961.]

---

923. *The Preparation of Silver Fluoroborate and Silver Hexafluorophosphate.*

By D. R. RUSSELL and D. W. A. SHARP.

SILVER salts of complex fluoro-acids are interesting because of their solubility in organic solvents and because of their potential use in organic and inorganic syntheses.[1] Silver fluoroborate has previously been prepared by the use of bromine trifluoride [2] or sulphur tetrafluoride [3] and from silver(I) fluoride and boron trifluoride in nitromethane,[4] hydrogen fluoride,[5] and benzene.[6] Silver hexafluorophosphate has been prepared by use of bromine trifluoride.[7] These salts tenaciously retain organic and other solvents, and the products of these reactions have to be heated to remove excess of solvent.

Both silver salts are readily obtained pure from silver(I) fluoride and boron trifluoride or phosphorus pentafluoride by use of sulphur dioxide as solvent. The solvent may easily be removed without heating by use of a simple vacuum line and the salts are obtained as clean dry products.

Experimental.—Silver fluoride was prepared by the method of Andersen, Bak, and Hillebert.[8] Boron trifluoride was a gift from the Imperial Smelting Corporation and was dried and purified by passage through a suspension of boric oxide in sulphuric acid. Phosphorus pentafluoride was obtained by heating a diazonium hexafluorophosphate (Phosfluorogen A). Sulphur dioxide was dried by passage over phosphorus pentoxide.

The gaseous fluoride was bubbled through a suspension of silver fluoride in liquid sulphur dioxide. When dissolution was complete the liquid was filtered free from insoluble impurities and evaporated to dryness *in vacuo*; no external heating was necessary. *X*-Ray powder photographs confirmed the identity of the products [(*a*) Found: Ag, 55·0. Calc. for $AgBF_4$: Ag, 55·4. (*b*) Found: Ag, 43·0. Calc. for $AgPF_6$: Ag, 42·7%].

[1] See, *e.g.*, Sharp, *Adv. Fluorine Chem.*, 1960, **1**, 68.
[2] Sharpe, *J.*, 1952, 4538.
[3] Kemmitt and Sharp, *J.*, 1961, 2496.
[4] Olah and Quinn, *J. Inorg. Nuclear Chem.*, 1960, **14**, 295.
[5] Clifford and Kongpricha, *J. Inorg. Nuclear Chem.*, 1957, **5**, 76.
[6] Heyns and Paulsen, *Angew. Chem.*, 1960, **72**, 349.
[7] Woolf and Emeléus, *J.*, 1950, 1050.
[8] Andersen, Bak, and Hillebert, *Acta Chem. Scand.*, 1953, **7**, 236.

We thank the Department of Scientific and Industrial Research for a maintenance grant (D. R. R.).

INORGANIC CHEMISTRY RESEARCH LABORATORIES,
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.7.

[*Received, June 2nd,* 1961.]

924. *The Reaction between Furfuryl Alcohol and 2,4-Dinitrophenylhydrazine in Methanolic Hydrochloric Acid.*

By K. G. LEWIS.

THE rearrangement of furfuryl alcohol by hydrogen chloride in methanol has been shown [1] to yield, among other substances, α-methoxylævulaldehyde dimethyl acetal, and not δ-methoxylævulaldehyde dimethyl acetal as previously suggested.[2,3] In a preliminary attempt to prepare the bis-2,4-dinitrophenylhydrazone of the supposed δ-methoxyaldehyde [3] for comparison with synthetic material of this structure, furfuryl alcohol was refluxed with a solution of 2,4-dinitrophenylhydrazine in methanolic hydrochloric acid. The mixture that formed was separable into substances (I), (II), and (III). Substance (I) was methyl lævulate 2,4-dinitrophenylhydrazone. Substance (II) was yellow and had m. p. 217—218°. The possibility that it was furfuraldehyde 2,4-dinitrophenylhydrazone (yellow form,[4] m. p. 212—214°), formed by oxidation of the furfuryl alcohol by 2,4-dinitrophenylhydrazine as suggested for certain unsaturated alcohols by Braude and Forbes,[5] was eliminated by comparison with the authentic furfuraldehyde derivative and by analysis. Analysis also showed that this material, although of similar m. p. to that recorded by Deriaz *et al.*[3] for the supposed δ-methoxylævulaldehyde bis-2,4-dinitrophenylhydrazone, could not have this structure. The derived molecular formula, $C_{17}H_{16}N_8O_9$, agreed with a formulation as lævulic acid 2,4-dinitrophenylhydrazide 2,4-dinitrophenylhydrazone and this was confirmed by a synthesis of this substance from lævuloyl chloride and 2,4-dinitrophenylhydrazine. Some lævulic acid derivatives may exist in cyclic form,[6] but it is likely that bis-derivatives, *e.g.*, the anil-anilide,[7] are derivatives of the open-chain form. While ultraviolet absorption spectra of compound (II) gave little useful information concerning the structure, the infrared spectrum (KCl disc) showed, in addition to the usual peak characteristic of the C=N grouping, a peak at 1680 cm.$^{-1}$ assigned to the carbonyl group of the acid hydrazide (Barton and Hendricksen [8] record 1678 cm.$^{-1}$ for an analogous group). Thus substance (II) must have the open-chain structure, R·NH·N:CMe·$[CH_2]_2$·CO·NH·NHR, where R = 2,4-$(NO_2)_2C_6H_3$.

The red substance (III), $C_{17}H_{14}N_8O_8$, was sparingly soluble in most solvents except nitrobenzene. It gave a very intense, broad ultraviolet maximum at 400—460 mμ characteristic of the bis-2,4-dinitrophenylhydrazones of conjugated alkenediones [9] and was shown by comparison to be 4-oxopent-2-enal bis-2,4-dinitrophenylhydrazone which has been observed to be formed [1] when α-methoxylævulaldehyde dimethyl acetal is treated with 2,4-dinitrophenylhydrazine in methanolic acid.

Experimental.—Reaction between furfuryl alcohol and 2,4-dinitrophenylhydrazine. Freshly distilled furfuryl alcohol (1 g.) was added to a boiling solution of 2,4-dinitrophenylhydrazine

[1] Lewis, *J.*, 1957, 531; Birkofer and Dutz, *Annalen*, 1957, **608**, 7.
[2] Pummerer and Gump, *Ber.*, 1923, **56**, 999; Pummerer, Guyot, and Birkofer, *Ber.*, 1935, **68**, 480.
[3] Deriaz, Stacey, Teece, and Wiggins, *J.*, 1949, 1222.
[4] Bredereck, *Ber.*, 1932, **65**, 1833.
[5] Braude and Forbes, *J.*, 1951, 1762.
[6] Cason and Reist, *J. Org. Chem.*, 1958, **23**, 1492; Lukes and Prelog, *Chem. Listy*, 1930, **24**, 251 (*Chem. Abs.*, 1930, **24**, 4762).
[7] Lukes and Linhartova, *Coll. Czech. Chem. Comm.*, 1960, **25**, 502.
[8] Barton and Hendrickson, *J.*, 1956, 1028.
[9] Lewis, *J.*, 1956, 1083.

(4 g.) in methanol (400 ml.) containing hydrochloric acid (4 ml.), and the mixture was refluxed for 2 hr. The precipitated material was filtered off and washed with cold methanol. The combined filtrate and washings were evaporated to 100 ml. and chilled. The brown crystals that separated were filtered off and recrystallised from methanol–dioxan, to give methyl lævulate 2,4-dinitrophenylhydrazone (I), m. p. and mixed m. p. 139—141°. The crude residue (*ca.* 2·5 g.) was boiled with methanol (500 ml.), and the boiling solution was filtered. The filtrate, on cooling, deposited small yellow crystals (m. p. 215°) of substance (II). This methanol extraction was repeated until the insoluble residue (III) appeared clear red. The combined crops of compound (II) were recrystallised from ethyl acetate, to give *lævulic acid* 2,4-*dinitrophenylhydrazide* 2,4-*dinitrophenylhydrazone*, m. p. 217—218° (decomp.) (Found: C, 42·9; H, 3·5; N, 23·1; OMe, 0. $C_{17}H_{16}N_8O_9$ requires C, 42·85; H, 3·4; N, 23·5%), $\lambda_{max.}$ 350 mμ (log ε 4·47) in dioxan. In the same solvent lævulic acid 2,4-dinitrophenylhydrazone showed $\lambda_{max.}$ 358 mμ (log ε 4·24), and *N*-acetyl-2,4-dinitrophenylhydrazine $\lambda_{max.}$ 330 mμ (log ε 4·17). The red residue (III) on recrystallisation from nitrobenzene–tetrachloroethane gave 4-oxopent-2-enal bis-2,4-dinitrophenylhydrazone, m. p. 265—266° (decomp.) (Found: C, 44·9; H, 3·3; O, 27·9; N, 24·6. Calc. for $C_{17}H_{14}N_8O_8$: C, 44·5; H, 3·1; O, 27·95; N, 24·45%). There was no depression of m. p. on admixture with authentic material.

Synthesis of lævulic acid 2,4-*dinitrophenylhydrazide* 2,4-*dinitrophenylhydrazone*. Lævuloyl chloride [10] (0·5 ml.), b. p. 74—78°/11 mm., was added to 2,4-dinitrophenylhydrazine (2 g.) in tetralin (50 ml.; distilled over sodium) at 160°. The temperature was kept at 150° for 30 min. and the mixture then left overnight. The product which had separated was filtered off and washed with benzene. The crude material was digested with ethyl acetate and crystallised thrice from acetic acid, to yield lævulic acid 2,4-dinitrophenylhydrazide 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 218° (decomp.) (Found: C, 42·9; H, 3·4; N, 23·5%).

THE UNIVERSITY OF NEW ENGLAND,
ARMIDALE, N.S.W., AUSTRALIA.

[*Received, June 5th*, 1961.]

[10] Clemo and Ramage, *J.*, 1931, 54.

---

925. *The Synthesis of* 4,5,7-*Trimethoxy*-2-*propylanthraquinone.*

By A. J. BIRCH and C. J. MOYE.

NALGIOVENSIN has been formulated [1] as 4,5-dihydroxy-2-2′-hydroxypropyl-7-methoxyanthraquinone, and to provide further support for this structure we have synthesised the substance named in the title, which is obtainable by a series of processes from nalgiovensin.

The process followed closely that used for the corresponding 2-methylanthraquinone derivative.[2] 3,5-Dimethoxyphthalic anhydride was condensed with 3-propylphenol by the Friedel–Crafts procedure and the product was brominated and cyclised in the standard manner.[3] Refluxing the cyclised product with hydriodic acid removed the bromine and gave the anthrone, which was oxidised by chromic acid to 4,5,7-trihydroxy-2-propylanthraquinone with the m. p. recorded [4] for the substance obtained similarly from nalgiovensin. Methylation to 4,5,7-trimethoxy-2-propylanthraquinone gave a compound identical in infrared spectrum with the compound from nalgiovensin and undepressed in m. p. by it. Nalgiovensin therefore certainly contains a 2-n-propyl group, as predicted [1] by the acetic acid theory of biosynthesis.

Experimental.—4,5,7-*Trimethoxy*-2-*propylanthraquinone*. (i) To aluminium chloride (10 g.) suspended in stirred benzene was slowly added a warm solution of 3,5-dimethoxyphthalic anhydride (4 g.) in *m*-propylphenol (16 c.c.). After 12 hr. the mixture was stirred for 3 hr. at 50°, 2 hr. at 60°, and 3 hr. at 70° and then poured on ice (50 g.) and 2N-hydrochloric acid (50 c.c.). The product was taken up in ether and extracted with sodium hydrogen carbonate solution. Acidification of the extract, followed by crystallisation of the precipitate from aqueous methanol, gave 3,5-*dimethoxy*-2-(2-*hydroxy*-4-*propylbenzoyl*)*benzoic acid* (0·9 g.), m. p.

[1] Birch and Massy-Westropp, *J.*, 1957, 2215.
[2] Brockmann, Kluge, and Muxfeldt, *Chem. Ber.*, 1957, **90**, 2302.
[3] Anslow and Raistrick, *Biochem. J.*, 1941, **35**, 1008.
[4] Raistrick and Ziffer, *Biochem. J.*, 1951, **49**, 563.

229—233° (Found: C, 66·1; H, 5·9. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%). This was brominated by the procedure of Anslow and Raistrick [3] for the corresponding methyl compound, *i.e.*, in 10% w/v acetic acid, finally at 50° (2 hr.). The oily product crystallised under light petroleum (b. p. 30—40°) but melted unsharply at ~220°. The crystalline product (190 mg. from 250 mg.) was directly cyclised with oleum (3·5 c.c.; 7% of SO_3) and boric acid (0·35 g.) at 90° for 15 min. Addition of ice and filtration gave a red solid that crystallised from chloroform–methanol as tan-coloured needles (75 mg.), m. p. 166—174°. This product (35 mg.) in acetic acid (2 c.c.) was refluxed with hydriodic acid (*d* 1·7; 0·2 c.c.) and red phosphorus (30 mg.) for 3 hr. Filtration and cooling gave yellow needles (20 mg.). This anthranol in acetic acid (5 c.c.) was treated with chromium trioxide (20 mg.) in 50% acetic acid (0·6 c.c.) for 0·5 hr. at 60°. Extraction with chloroform and crystallisation from benzene gave orange-yellow crystals (10 mg.), m. p. 213—217° (recorded m. p. for 4,5,7-trihydroxy-2-propylanthraquinone, 216·5—217°). Methylation with potassium carbonate and methyl sulphate in acetone, chromatography on alumina in ether, and crystallisation from benzene–light petroleum (b. p. 40—60°) gave *4,5,7-trimethoxy-2-propylanthraquinone* (5 mg.), m. p. 169—170°, undepressed by the substance described below and identical with it in infrared spectrum (Found: C, 70·7; H, 6·1. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%).

(ii) Reduction of nalgiovensin as described in the literature,[4] oxidation with chromic acid (4 equiv.) in acetic acid, and methylation of the product with a large excess of methyl sulphate and aqueous sodium hydroxide gave a brown gum. This was taken up in benzene; tar was precipitated on addition of light petroleum (b. p. 40—60°). The product then obtained by evaporation was chromatographed in ether on alumina (grade H; neutralised with acetic acid) and recrystallised from light petroleum (b. p. 60—80°). 4,5,7-Trimethoxy-2-propylanthraquinone had m. p. 169—170°.

We are indebted to Professor H. Brockmann for communicating experimental procedures in advance of their publication.

Department of Chemistry, University of Manchester. [*Received, June 7th,* 1961.]

---

926. *The Synthesis of* (±)-S-3-*Methylbut-2-enylhomocysteine.*

By A. J. Birch and M. Slaytor.

We have postulated[1] the biochemical introduction of isoprenoid groups (including isopentenyl groups) into phenolic and related compounds by a process analogous to biological *C*-methylation. Since the latter undoubtedly results from the action of "active" methionine,[2] which acts as a methyl-cation donor, we were led to postulate a similar source of isopentenyl cations. This now appears to be isopentenyl pyrophosphate,[3] from which, however, the group could conceivably be transferred to other biologically active centres containing thiol groups. We have accordingly synthesised the isopentenyl analogue of methionine, namely, (±)-*S*-3-methylbut-2-enylhomocysteine.

Experimental.—3-Methylbut-2-enyl bromide[4] (1·5 g., 0·01 mole) was added to a solution of (±)-*S*-benzylhomocysteine[5] (2·25 g., 0·01 mole) in liquid ammonia (50 c.c.) to which enough sodium had been added to give a permanent blue colour.[6] The ammonia was allowed to evaporate, water (10 c.c.) was added, and the solution neutralised with hydriodic acid until it was alkaline to Congo Red but acid to litmus paper; (±)-S-3-*methylbut-2-enylhomocysteine* crystallised. It recrystallised from water as plates (1·25 g., 64%), m. p. 207° (Found: C, 53·2; H, 8·15. $C_9H_{17}NO_2S$ requires C, 53·2; H, 8·43%).

We are indebted to the Nuffield Foundation (Australia) for financial assistance.

Department of Organic Chemistry, University of Sydney, N.S.W., Australia. [*Received, June 7th,* 1961.]

[1] Birch, Elliott, and Penfold, *Austral. J. Chem.*, 1954, **7**, 169.
[2] Birch, English, Massy-Westropp, Slaytor, and Smith, *J.*, 1958, 365.
[3] See, *e.g.*, Lynen, Eggerer, Henning, and Kessel, *Angew. Chem.*, 1958, **70**, 738.
[4] Staudinger, Kreis, and Schilt, *Helv. Chim. Acta*, 1922, **5**, 750.
[5] Patterson and du Vigneaud, *J. Biol. Chem.*, 1935, **111**, 393.
[6] Challenger and Dransfield, *J.*, 1955, 1153.

XUM

XUM

THE CHEMICAL SOCIETY

Patron

Her Majesty the Queen

President

Sir Alexander Todd, M.A., D.Sc., F.R.S.

Vice-Presidents

who have filled the office of President

H. J. Emeléus, C.B.E., M.A., D.Sc., F.R.S.
Sir Cyril Hinshelwood, O.M., M.A., Sc.D., F.R.S.
E. L. Hirst, C.B.E., D.Sc., LL.D., F.R.S.
Sir Christopher Ingold, D.Sc., F.R.I.C., F.R.S.
Sir Eric Rideal, M.B.E., M.A., D.Sc., F.R.S.
Sir Robert Robinson, O.M., D.Sc., LL.D., F.R.S.

Vice-Presidents

F. Bergel, D.Sc., F.R.I.C., F.R.S.
E. J. Bowen, M.A., D.Sc., F.R.S.
E. R. H. Jones, D.Sc., F.R.I.C., F.R.S.
J. M. Robertson, M.A., D.Sc., F.R.S.
M. Stacey, Ph.D., D.Sc., F.R.S.

Honorary Treasurer

J. W. Barrett, Ph.D., A.R.C.S., F.R.I.C.

Honorary Secretaries

J. Chatt, M.A., Sc.D., F.R.S.
A. W. Johnson, Sc.D., Ph.D., A.R.C.S.
K. W. Sykes, M.A., D.Phil.

Ordinary Members of Council

C. B. Amphlett, Ph.D., D.Sc.
G. O. Aspinall, D.Sc., Ph.D., F.R.I.C.
L. J. Bellamy, B.Sc., Ph.D.
G. E. Coates, M.A., D.Sc., F.R.I.C.
W. Cocker, M.A., D.Sc., F.R.I.C., M.R.I.A.
D. P. Craig, M.Sc., D.Sc.
D. H. Everett, M.B.E., M.A., D.Phil.
I. J. Faulkner, Ph.D., F.R.I.C.
W. Gerrard, D.Sc., Ph.D., F.R.I.C.
C. H. Hassall, M.Sc., Ph.D., F.R.I.C.
R. N. Haszeldine, M.A., Sc.D., F.R.I.C.
A. K. Holliday, Ph.D., D.Sc., F.R.I.C.
J. Honeyman, Ph.D., D.Sc.
A. H. Lamberton, Ph.D.
J. W. Linnett, M.A., D.Phil., F.R.S.
E. A. Moelwyn-Hughes, D.Phil., D.Sc., Sc.D.
H. T. Openshaw, M.A., D.Phil.
H. M. Powell, B.Sc., M.A., F.R.S.
R. A. Raphael, Ph.D., D.Sc., F.R.I.C.
J. C. Robb, D.Sc., Ph.D.
W. A. Waters, Sc.D., F.R.I.C., F.R.S.

Ex Officio

J. W. Cook, D.Sc., F.R.I.C., F.R.S. (Chairman of the Chemical Council)
D. H. Hey, D.Sc., F.R.I.C., F.R.S. (Chairman of the Publication Committee)
E. D. Hughes, D.Sc., F.R.I.C., F.R.S. (Chairman of the Joint Library Committee)

General Secretary

J. R. Ruck Keene, M.B.E., T.D., M.A.

Librarian

R. G. Griffin, F.L.A.

XUM

TABLES OF INTERATOMIC DISTANCES AND CONFIGURATION IN MOLECULES AND IONS

(Special Publication No. 11)

Compiled by: H. J. M. Bowen, M.A., D.Phil., J. Donohue, M.A., Ph.D., D. G. Jenkin, M.Sc., Olga Kennard, M.A., A.Inst.P., P. J. Wheatley, M.A., D.Phil., and D. H. Whiffen, M.A., D.Phil.

Scientific Editor: L. E. Sutton, M.A., D.Phil., F.R.S.

Assistant Scientific Editor: D. G. Jenkin, M.Sc.

General Editors: A. D. Mitchell, D.Sc., F.R.I.C.
L. C. Cross, Ph.D., A.R.C.S., F.R.I.C.

Cloth Bound. 384 pp. Size 9¾" × 7"
Price: £2. 2s. 0d. (U.S.A. $6)

THE CHEMICAL SOCIETY
BURLINGTON HOUSE, LONDON, W.1

Printed in Great Britain by Richard Clay and Company, Ltd., Bungay, Suffolk.

XUM

XUM